



A 33-year-old woman comes to a fertility clinic for evaluation. She has been attempting to conceive for 1 year with her current partner of 5 years without success. Her monogamous partner has been found to have adequate sperm motility, volume, and count. The patient used oral contraceptives for 15 years but stopped a year ago. Seven years ago, she received ceftriaxone for fever, abdominal pain, and vaginal discharge. Which of the following is the most likely major contributing factor to her inability to conceive?

- ☐ A. Advanced maternal age
- ☐ B. Congenital absence of the vas deferens
- ☐ C. Inadequate time for attempted conception
- ☐ D. Insufficient antibiotic therapy
- ☐ E. Long-term oral contraceptive use

**Submit**





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- ☐ A. Advanced maternal age (2%)
- ☐ B. Congenital absence of the vas deferens (0%)
- ☐ C. Inadequate time for attempted conception (4%)
- ☒ D. Insufficient antibiotic therapy (78%)
- ☐ E. Long-term oral contraceptive use (13%)

Correct



78%

Answered correctly



01 min, 11 secs

Time Spent



09/12/2020

Last Updated





Mark



Previous



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Tutorial



Lab Values



Notes



Calculator



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Settings

Pelvic inflammatory disease	
Symptoms	<ul style="list-style-type: none"><li>• Lower abdominal pain</li><li>• Abnormal bleeding</li></ul>
Physical examination	<ul style="list-style-type: none"><li>• Cervical motion tenderness</li><li>• Fever &gt;38.3 C (&gt;100.9 F)</li><li>• Mucopurulent cervical discharge</li></ul>
Treatment	<ul style="list-style-type: none"><li>• Third-generation cephalosporin <b>plus</b></li><li>• Azithromycin <b>or</b> doxycycline</li></ul>
Complications	<ul style="list-style-type: none"><li>• Tubo-ovarian abscess</li><li>• Infertility</li><li>• Ectopic pregnancy</li><li>• Perihepatitis</li></ul>

**Pelvic inflammatory disease (PID)** is most frequently caused by *Neisseria gonorrhoeae* and *Chlamydia*



0



Feedback



Suspend



End Block



**Pelvic inflammatory disease (PID)** is most frequently caused by *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. Infection by both organisms can be asymptomatic or cause PID or **cervicitis**. PID involves inflammation of the endometrium, fallopian tubes, and/or peritoneal cavity (eg, Fitz-Hugh-Curtis syndrome). PID is the most common cause of **tubal-factor infertility**. **Ectopic pregnancy** is another potential significant consequence of untreated infection and tubal scarring.

This patient's history of fever, abdominal pain, and discharge is highly characteristic of PID. Treatment must always include coverage of both *C trachomatis* and *N gonorrhoeae* as **coinfection** is common. A third-generation **cephalosporin** will treat the gonococcal infection, and further treatment with **azithromycin or doxycycline** is required to treat the chlamydia, which is not sensitive to beta-lactams. This patient was treated with only a cephalosporin (eg, ceftriaxone), and she likely had an ongoing asymptomatic or subclinical infection. Even if adequate treatment was provided, long-term sequelae may not have been prevented due to scarring and adhesion formation from the healing of inflamed tissues. As a result, this patient likely had **fallopian tube** scarring/occlusion, loss of ciliary action, and subsequent infertility.

**(Choice A)** Advanced maternal age is an important factor contributing to decreased fertility as women approach menopause (average age 51). The decrease in fecundity after age 35 is primarily due to the diminishing quantity and quality of oocytes.

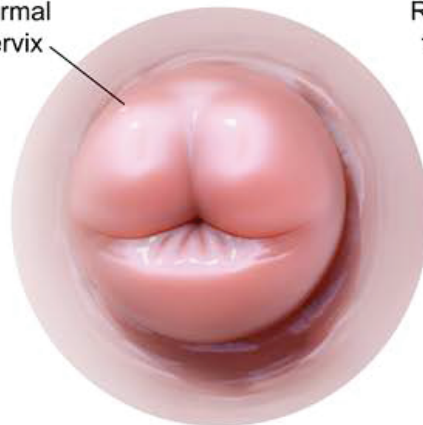




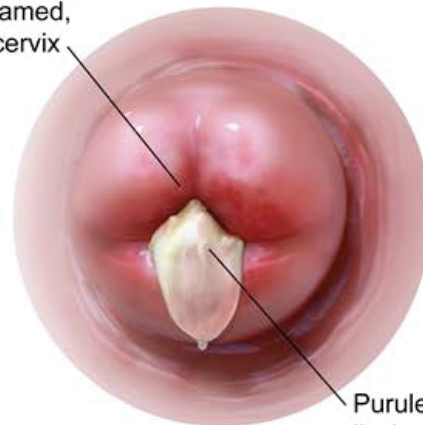
Pelvic inflammatory disease (PID) is most frequently caused by *Neisseria gonorrhoeae* and *Chlamydia*

## Exhibit Display

## Cervicitis

Normal  
cervix

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Red, inflamed,  
friable cervixPurulent  
discharge

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Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



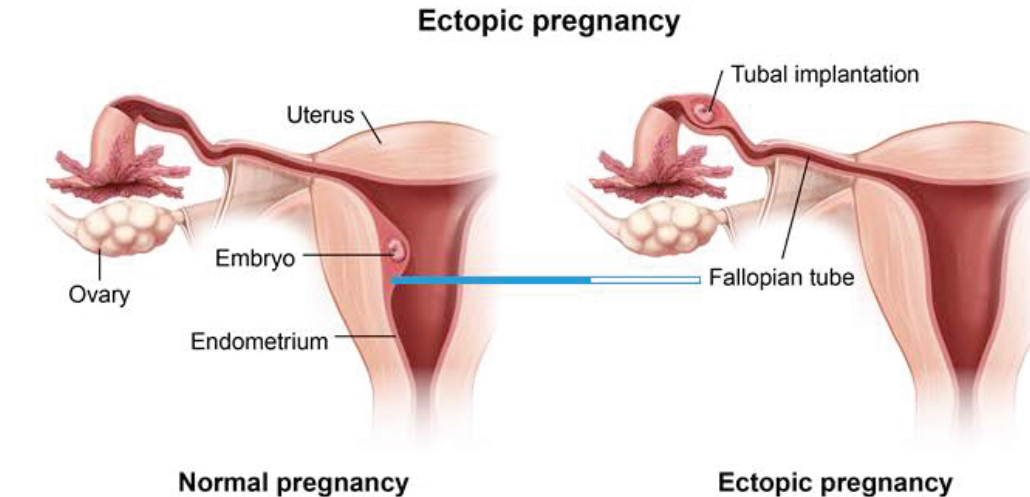
Text Zoom



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Pelvic inflammatory disease (PID) is most frequently caused by *Neisseria gonorrhoeae* and *Chlamydia*

Exhibit Display



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**(Choice B)** Congenital absence of the vas deferens is characterized by low sperm volume and acidic pH of an ejaculate sample. This patient's partner has adequate sperm volume and is therefore unlikely to have congenital absence of the vas deferens.

**(Choice C)** This patient has been attempting to conceive for 1 year. Most couples having unprotected intercourse will successfully conceive within 1 year.

**(Choice E)** Oral contraceptive use is not associated with ovarian failure. The menstrual cycle and fertility should return to normal shortly after the contraceptive is discontinued. However, premature ovarian failure (eg, primary ovarian insufficiency) can occur in women who smoke or those receiving radiation or chemotherapy.

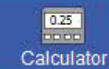
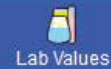
### Educational objective:

Pelvic inflammatory disease (PID) is most frequently caused by *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. Severe or inadequately treated PID can result in fallopian tube scarring, which in turn can lead to infertility. Treatment must always include coverage of both organisms with a third-generation cephalosporin (eg, ceftriaxone) as well as azithromycin or doxycycline.

### References

- [Screening for chlamydia and gonorrhea: U.S. Preventive Services Task Force recommendation](#)

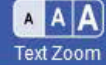
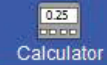
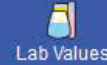
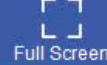




A 38-year-old Caucasian female presents to your office for a routine check-up, and requests a simple and reliable method of contraception. She remarks, "I have already had three children. I would not like to have more any time soon. Do you think I could start on birth control pills?" She has no significant past medical history, and does not take any medications other than a daily multivitamin. Her family history is significant for stroke in her mother and type 2 diabetes mellitus in her father. Which of the following factors would most affect your decision to prescribe oral contraceptives to this patient?

- ☐ A. Diet
- ☐ B. Physical activity level
- ☐ C. Smoking status
- ☐ D. Parity
- ☐ E. Glucose intolerance
- ☐ F. Serum HDL level

**Submit**



A 38-year-old Caucasian female presents to your office for a routine check-up, and requests a simple and reliable method of contraception. She remarks, "I have already had three children. I would not like to have more any time soon. Do you think I could start on birth control pills?" She has no significant past medical history, and does not take any medications other than a daily multivitamin. Her family history is significant for stroke in her mother and type 2 diabetes mellitus in her father. Which of the following factors would most affect your decision to prescribe oral contraceptives to this patient?

- ☐ A. Diet (1%)
- ☐ B. Physical activity level (1%)
- ✓ ☒ C. Smoking status (81%)
- ☐ D. Parity (3%)
- ☐ E. Glucose intolerance (3%)
- ☐ F. Serum HDL level (7%)







Mark



Previous



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Full Screen



Tutorial



Lab Values



Notes



Calculator



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Settings

When taken as prescribed, oral contraceptive pills are a reliable and reversible form of female contraception. They typically contain a combination of estrogen and progestin, and are taken in cycles interrupted by menstrual bleeding. The estrogen in oral contraceptives prevents pregnancy by suppressing the midcycle gonadotropin surge, thereby inhibiting ovulation. Progesterone is added to counteract the increased risk of endometrial cancer associated with unopposed effect of estrogen. Additionally, progesterone may enhance the contraceptive efficacy by decreasing the permeability of the cervical mucus to sperm.

Side effects of oral contraceptives may include: breakthrough menstrual bleeding, breast tenderness, and weight gain. Additionally, there is a risk of more serious, though rare, events, such as deep vein thrombosis, pulmonary embolism, ischemic stroke, and myocardial infarction. The risk of cardiovascular events due to oral contraceptive pills is increased in smokers and patients over the age of 35. In particular, individuals who smoke more than 15 cigarettes per day have a much higher incidence of cardiovascular events.

**(Choices A and B)** Use of oral contraceptive pills may cause weight gain. However, there is no relation of weight gain to the more serious potential health risks associated with oral contraceptives.



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Feedback



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End Block



**(Choices A and B)** Use of oral contraceptive pills may cause weight gain. However, there is no relation of weight gain to the more serious potential health risks associated with oral contraceptives.

**(Choice D)** The risks of oral contraceptive pills are similar in females regardless of past pregnancy or childbearing status.

**(Choice E)** Oral contraceptive pills can induce insulin resistance and cause glucose intolerance. However, the risk of glucose intolerance was most significant with the first generation of high-dose estrogen oral contraceptives. With the reduced quantities of estrogen in the newer 2<sup>nd</sup> and 3<sup>rd</sup> generation oral contraceptive pills, glucose intolerance has become much less common. Adequately controlled diabetes mellitus, in the absence of other cardiovascular risk factors, is not a contraindication to the use of oral contraception.

**(Choice F)** Although low HDL is a known cardiovascular risk factor, there is no data to suggest that patients with low HDL have especially heightened cardiovascular risks while using oral contraceptives. The guideline for oral contraceptive use in patients with hypercholesterolemia is dependent instead upon the LDL level. Oral contraceptives are generally safe to use in patients with an LDL below 160 mg/dL without any other cardiovascular risk factors.

**Educational Objective:**





contraception.

**(Choice F)** Although low HDL is a known cardiovascular risk factor, there is no data to suggest that patients with low HDL have especially heightened cardiovascular risks while using oral contraceptives. The guideline for oral contraceptive use in patients with hypercholesterolemia is dependent instead upon the LDL level. Oral contraceptives are generally safe to use in patients with an LDL below 160 mg/dL without any other cardiovascular risk factors.

### Educational objective:

The absolute contraindications to the use of OCPs are:

1. Prior history of thromboembolic event or stroke
2. History of an estrogen-dependent tumor
3. Women over age 35 years who smoke heavily
4. Hypertriglyceridemia
5. Decompensated or active liver disease (would impair steroid metabolism)
6. Pregnancy

### References

- Smoking increases the risk of venous thrombosis and acts synergistically with oral contraceptive use.







A 40-year-old woman, gravida 5, para 0, aborta 4, at 12 weeks gestation comes to the emergency department due to vaginal bleeding, midline pelvic pain, and severe nausea and vomiting. She has a history of 4 prior first trimester losses. Pelvic examination shows a 16-week-sized uterus. Speculum examination reveals dark red blood in the vagina. A  $\beta$ -hCG level is  $>100,000$  mIU/mL, and an ultrasound shows no fetus and a uterine cavity filled with multiple small cysts. The patient undergoes dilation and curettage in the operating room, and a friable mass of tissue consisting of many thin-walled cysts is evacuated from her uterus. Examination of the tissue would most likely show which karyotype?

- ☐ A. 46,XX
- ☐ B. 46,XY
- ☐ C. 47,XXX
- ☐ D. 47,XXY
- ☐ E. 69,XXX
- ☐ F. 69,XXY







department due to vaginal bleeding, midline pelvic pain, and severe nausea and vomiting. She has a history of 4 prior first trimester losses. Pelvic examination shows a 16-week-sized uterus. Speculum examination reveals dark red blood in the vagina. A  $\beta$ -hCG level is  $>100,000$  mIU/mL, and an ultrasound shows no fetus and a uterine cavity filled with multiple small cysts. The patient undergoes dilation and curettage in the operating room, and a friable mass of tissue consisting of many thin-walled cysts is evacuated from her uterus. Examination of the tissue would most likely show which karyotype?

☒ A. 46,XX (35%)

☒ B. 46,XY (19%)

☐ C. 47,XXX (4%)

☐ D. 47,XXY (5%)

☐ E. 69,XXX (11%)

☐ F. 69,XXY (23%)

Incorrect

Correct answer



35%



01 min, 21 secs

Time spent



01/31/2021

Last updated

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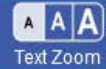
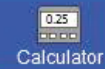
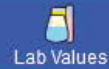
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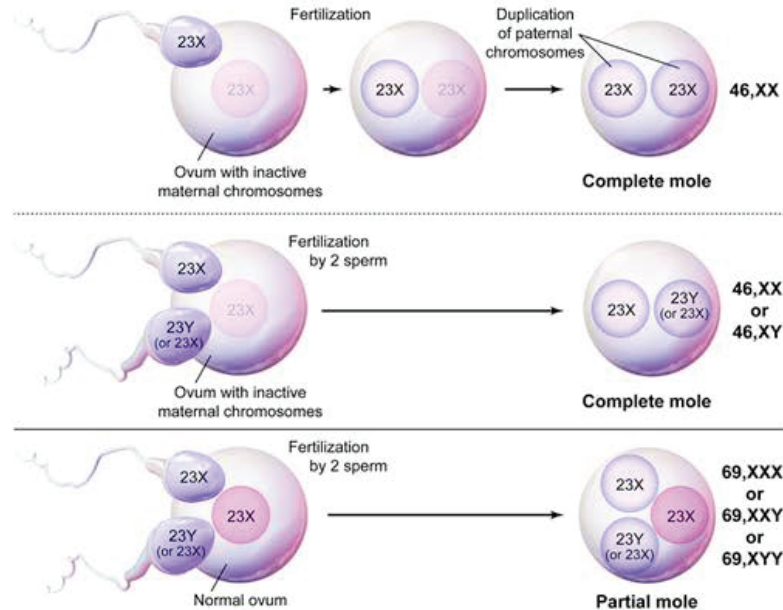


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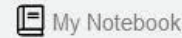
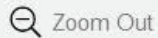
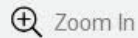


### Exhibit Display

#### Hydatidiform mole



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A molar pregnancy is a form of gestational trophoblastic disease and can be classified as complete or partial. A complete mole has **no fetal structures** and is composed entirely of large, edematous, and disordered chorionic villi that appear grossly as clusters of vesicular structures ("**bunch of grapes**"). This patient has a **complete hydatidiform mole**, which typically presents with pelvic pain and vaginal bleeding. The uterus is larger than expected for gestational age, and  $\beta$ -hCG levels are markedly elevated due to **trophoblastic hyperplasia**. An ultrasound demonstrates a central heterogenous mass with multiple cystic areas and is classically described as a "**Swiss cheese**" or "**snowstorm**" pattern. Risk factors for molar pregnancies include extremes of maternal age, prior molar pregnancy, prior miscarriage, or infertility.

A complete mole most commonly results from the fertilization of an ovum that has no maternal chromosomes (either due to absence or inactivation) by one sperm (90% of cases). The chromosomes from the haploid 23X sperm are then duplicated, forming diploid **46,XX** tissue that contains **only paternal DNA**. 46,YY moles from duplication of 23Y sperm have not been observed, as a zygote without an X chromosome would not survive. Less commonly, 2 sperm can fertilize an empty ovum and create 46,XY tissue (**Choice B**).

(**Choice C**) 47,XXX is the most common sex chromosome abnormality in females. It is usually diagnosed







Item 3 of 40

Question Id: 1830



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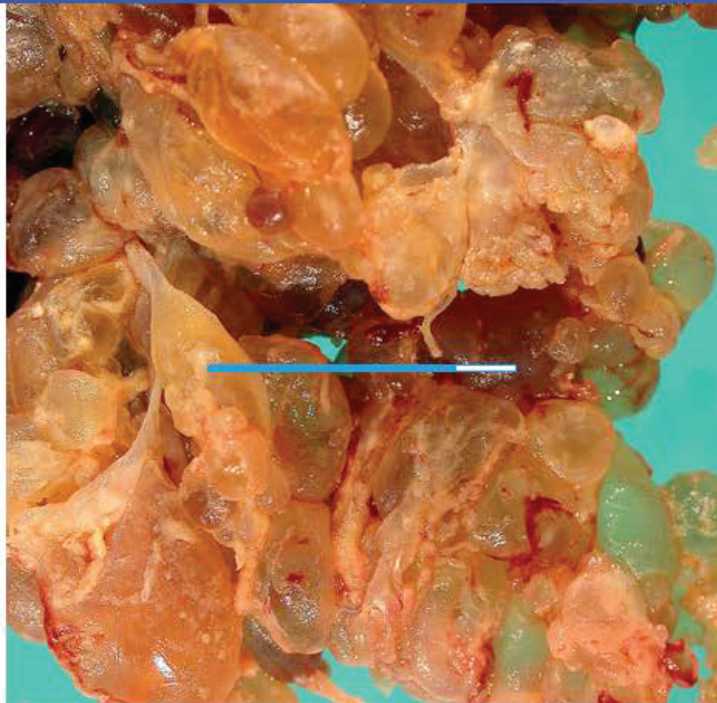


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### Exhibit Display



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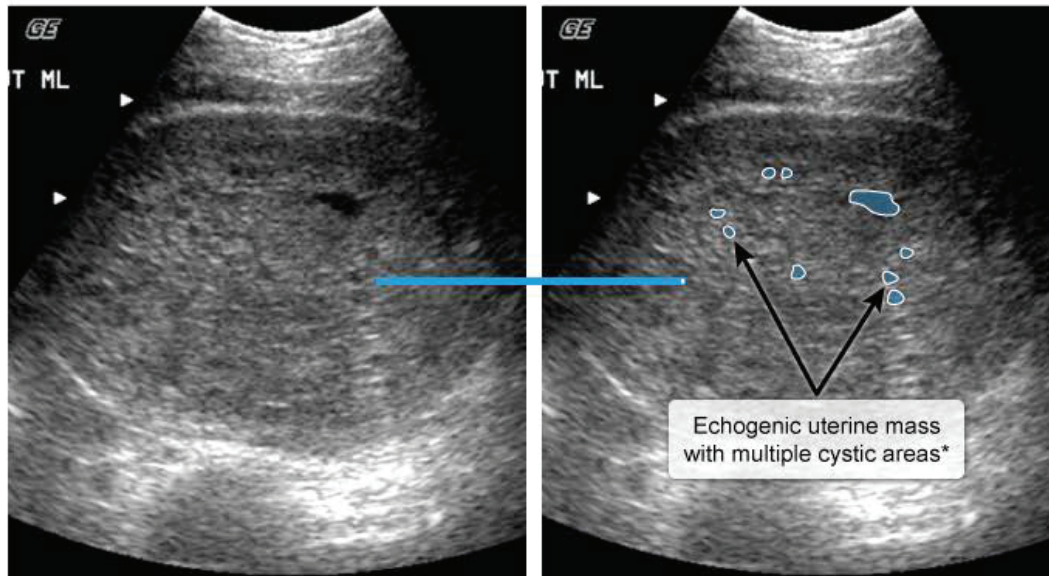
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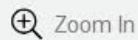
## Exhibit Display

## Complete hydatidiform mole

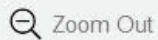


\*\*"Snowstorm" appearance

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chromosome would not survive. Less commonly, 2 sperm can fertilize an empty ovum and create 40,X1 tissue (**Choice B**).

(**Choice C**) 47,XXX is the most common sex chromosome abnormality in females. It is usually diagnosed incidentally during genetic testing as the carriers of this genotype are typically normal.

(**Choice D**) Klinefelter syndrome is associated with the 47,XXY karyotype and is associated with primary hypogonadism in males. It is likely due to nondisjunction of the sex chromosomes during meiotic division of the gamete of either parent.

(**Choices E and F**) Partial molar pregnancies have 69,XXX or 69,XXY karyotype as the result of fertilization of an ovum by 2 sperm. Partial moles typically contain fetal tissue and normal placental villi intermixed with hydropic villi.

### Educational objective:

A complete mole usually results when an empty ovum is fertilized by a haploid sperm. Subsequent duplication of the paternal genetic complement (23X) results in the characteristic 46,XX genotype.

### References

- [Gestational trophoblastic disease.](#)





A 24-year-old woman at 38 weeks gestation delivers healthy twins vaginally after a prolonged labor. Shortly after the placenta is delivered, profuse vaginal bleeding and a boggy uterus are noted on examination. Uterine massage and uterotonic medications, including oxytocin, fail to stop the bleeding. The patient is taken to the operating room for a laparotomy. Bilateral ligation of which of the following arteries is most likely to control her bleeding and preserve her fertility?

- ☐ A. Common iliac
- ☐ B. External iliac
- ☐ C. Internal iliac
- ☐ D. Internal pudendal
- ☐ E. Ovarian

Submit







A 24-year-old woman at 38 weeks gestation delivers healthy twins vaginally after a prolonged labor. Shortly after the placenta is delivered, profuse vaginal bleeding and a boggy uterus are noted on examination. Uterine massage and uterotonic medications, including oxytocin, fail to stop the bleeding. The patient is taken to the operating room for a laparotomy. Bilateral ligation of which of the following arteries is most likely to control her bleeding and preserve her fertility?

- ☐ A. Common iliac (1%)
- ☐ B. External iliac (3%)
- ☒ C. Internal iliac (58%)
- ☐ D. Internal pudendal (25%)
- ☐ E. Ovarian (10%)

Correct



58%

Answered correctly



15 secs

Time Spent

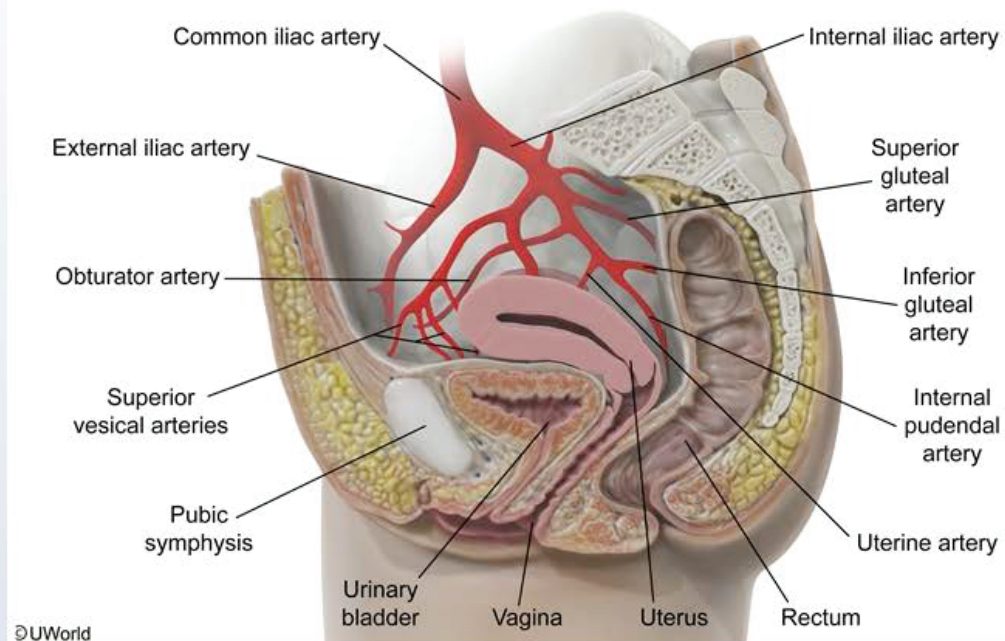


10/21/2020

Last Updated



### Branches of the internal iliac artery in the female



**Postpartum hemorrhage** is an obstetrical emergency and a leading cause of maternal mortality.

Postpartum hemorrhage is frequently caused by failure of the uterus to contract and compress the



**Postpartum hemorrhage** is an obstetrical emergency and a leading cause of maternal mortality.

Postpartum hemorrhage is frequently caused by failure of the uterus to contract and compress the placental site blood vessels. Risk factors include prolonged labor and twin gestation. These conditions lead to **uterine atony** (loss of uterine tone), characterized by a boggy uterus that cannot contract effectively after placental delivery. Surgery is indicated when medical management (uterine massage, uterotonic medications) of postpartum hemorrhage fails to control bleeding.

The pelvic organs are mainly supplied by the internal iliac arteries (also known as the hypogastric arteries).

The uterine arteries, the major blood supply to the uterus, are branches of the **internal iliac arteries**.

**Bilateral ligation** (eg, suturing) of the internal iliac arteries should **stop uterine blood flow** and hemorrhage, thereby preventing the need for hysterectomy. The uterus has collateral blood flow from the ovarian arteries, which is sufficient to maintain uterine function after internal iliac ligation. Structures that are supplied by other branches of the internal iliac arteries have collateral circulation as well.

**(Choices A and B)** The aorta splits into the right and left common iliac arteries, which split into the internal and external iliac arteries. The external iliac artery becomes the femoral artery after it exits the pelvis and supplies the leg. Ligation of the common iliac artery would truncate blood supply to the pelvis and lower







are supplied by other branches of the internal iliac arteries have collateral circulation as well.

**(Choices A and B)** The aorta splits into the right and left common iliac arteries, which split into the internal and external iliac arteries. The external iliac artery becomes the femoral artery after it exits the pelvis and supplies the leg. Ligation of the common iliac artery would truncate blood supply to the pelvis and lower extremity. Ligation of the external iliac artery would cut off blood flow to the lower extremity but not affect uterine blood flow.

**(Choice D)** The internal pudendal artery branches off the anterior trunk of the internal iliac artery and runs through the sciatic foramina to supply blood to the perineum. Ligation of the internal pudendal artery would not affect uterine blood flow. Injury to the pudendal artery during vaginal delivery can cause a vulvar hematoma.

**(Choice E)** The uterus receives collateral blood supply from the ovarian artery, which runs from the abdominal aorta through the infundibulopelvic ligament (suspensory ligament) to supply the ovary. Ligation of the ovarian artery would risk necrosis of the ovaries and infertility. Blood flow through the ovarian artery is compromised during ovarian torsion.

### Educational objective:

Postpartum hemorrhage is an obstetrical emergency. Bilateral ligation of the internal iliac artery can





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### Educational objective:

Postpartum hemorrhage is an obstetrical emergency. Bilateral ligation of the internal iliac artery can decrease uterine blood flow and control postpartum hemorrhage that is unresponsive to medical management (eg, uterine massage, uterotonic medications).

### References

- [Pelvic arterial ligations for severe post-partum hemorrhage. Indications and techniques.](#)





A 34-year-old African American woman, gravida 3 para 3, comes to the office for increasing pelvic pressure. For the past year, the patient has had chronic, dull pelvic pressure. In addition, she has had increased urinary frequency, but no dysuria or hematuria. The patient has no chronic medical conditions and no prior surgeries. She had 3 term vaginal deliveries in her 20s and is currently using a progestin-only contraceptive. The patient has 3-4 days of monthly menstrual bleeding. She follows a vegan diet and works in a textile factory. There is a family history of ovarian cancer. Blood pressure is 112/68 mm Hg and pulse is 64/min. Cardiopulmonary examination is normal. The abdomen is soft, nontender, and nondistended. There is a palpable, irregular mass slightly above the pubic symphysis. On pelvic examination, the cervix has no lesions and the uterus is irregularly enlarged and mobile. Urinalysis is normal. Which of the following is the most likely risk factor for this patient's clinical presentation?

- ☐ A. Family history of ovarian cancer
- ☐ B. Occupational exposure in a textile factory
- ☒ C. Prior vaginal deliveries
- ☐ D. Progestin-only contraception use
- ☐ E. Race







and no prior surgeries. She had 5 term vaginal deliveries in her 20s and is currently using a progestin-only contraceptive. The patient has 3-4 days of monthly menstrual bleeding. She follows a vegan diet and works in a textile factory. There is a family history of ovarian cancer. Blood pressure is 112/68 mm Hg and pulse is 64/min. Cardiopulmonary examination is normal. The abdomen is soft, nontender, and nondistended. There is a palpable, irregular mass slightly above the pubic symphysis. On pelvic examination, the cervix has no lesions and the uterus is irregularly enlarged and mobile. Urinalysis is normal. Which of the following is the most likely risk factor for this patient's clinical presentation?

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- ☐ C. Prior vaginal deliveries
- ☐ D. Progestin-only contraception use
- ☐ E. Race
- ☐ F. Vegan diet

**Submit**

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- ☐ A. Family history of ovarian cancer (20%)
- ☐ B. Occupational exposure in a textile factory (11%)
- ☐ C. Prior vaginal deliveries (9%)
- ☐ D. Progestin-only contraception use (19%)
- ☒ E. Race (38%)
- ☐ F. Vegan diet (0%)



### Uterine leiomyomas (fibroids)

#### Clinical features

- Heavy, prolonged menses
- Pressure symptoms
  - Pelvic pain
  - Constipation
  - Urinary frequency
- Obstetric complications
  - Impaired fertility
  - Pregnancy loss
  - Preterm labor
- Enlarged, irregular uterus

#### Workup

- Ultrasound

#### Treatment

- Asymptomatic: observation
- Symptomatic: CHC, surgery







This patient with an **irregularly enlarged uterus** likely has **uterine leiomyomas**, more commonly known as fibroids. Uterine fibroids are benign, monoclonal smooth muscle tumors that develop within the uterine myometrium. Depending on their size and location, **leiomyomas** may cause heavy menses (due to increased endometrial surface area), obstetric complications, and bulk symptoms (eg, **chronic pelvic pressure, urinary frequency**, constipation).

Uterine leiomyomas are relatively common (up to 25%) in reproductive-age women. The differing prevalence, size, and symptom severity among patients likely depends on multiple factors such as family history and race. **African American women** are 2-3 times more likely than Caucasian women to develop fibroids, and symptom onset typically occurs earlier (eg, mid to late 20s). This may be due to African American women having an early age of menarche, which is an additional risk factor for fibroid development.

Diagnosis is confirmed by ultrasound. Treatment can be either medical (eg, combined estrogen-progestin contraceptive pills) or surgical (eg, hysterectomy).

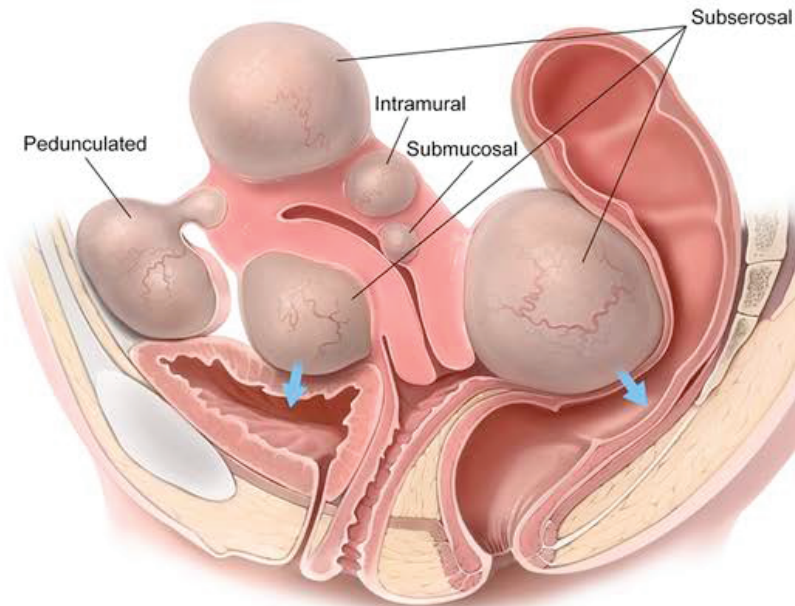
**(Choice A)** A family history of ovarian cancer increases the risk for ovarian cancer in those with *BRCA 1* and *2* gene mutations. Patients with ovarian cancer can present with bulk symptoms; however, examination typically reveals large, immobile ovaries. There is no correlation between a family history of



This patient with an irregularly enlarged uterus likely has uterine leiomyomas, more commonly known

### Exhibit Display

#### Uterine fibroids



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Zoom In

Zoom Out

Reset

New | Existing

My Notebook



ovarian cancer and fibroids.

**(Choice B)** Working in a textile factory can be a risk factor for bladder cancer due to occupational exposure to chemical carcinogens. Patients with bladder cancer can present with increased urinary frequency but typically have concomitant hematuria.

**(Choice C)** Prior deliveries (ie, increased parity) increase the risk of adenomyosis, or endometrial tissue within the myometrium. **Adenomyosis** may present with pelvic pressure; however, patients typically have a symmetrically enlarged, tender, globular uterus. Increased parity may decrease the risk of fibroids.

**(Choice D)** Progestin-only contraception may decrease fibroid size and can be used to treat symptomatic fibroids. It is not a risk factor for fibroid development.

**(Choice F)** Some environmental factors, such as increased red meat consumption, may increase the risk of uterine fibroids. A vegan diet has not been associated with an increased risk.

### Educational objective:

Uterine leiomyoma (ie, fibroids) can present with bulk symptoms (eg, pelvic pressure, urinary frequency) and an irregularly enlarged uterus. African American women are at increased risk of developing fibroids.

### References



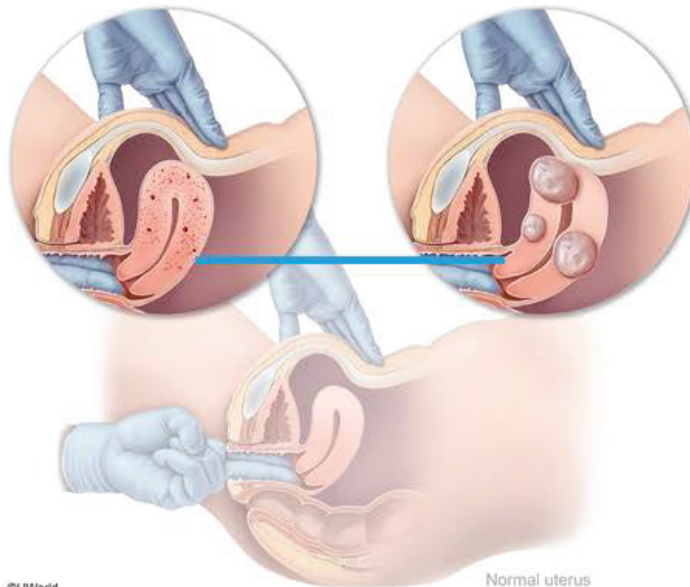


## Exhibit Display

## Adenomyosis vs fibroids

**Adenomyosis**  
Diffusely enlarged, tender uterus

**Fibroids**  
Irregularly enlarged uterus



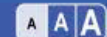
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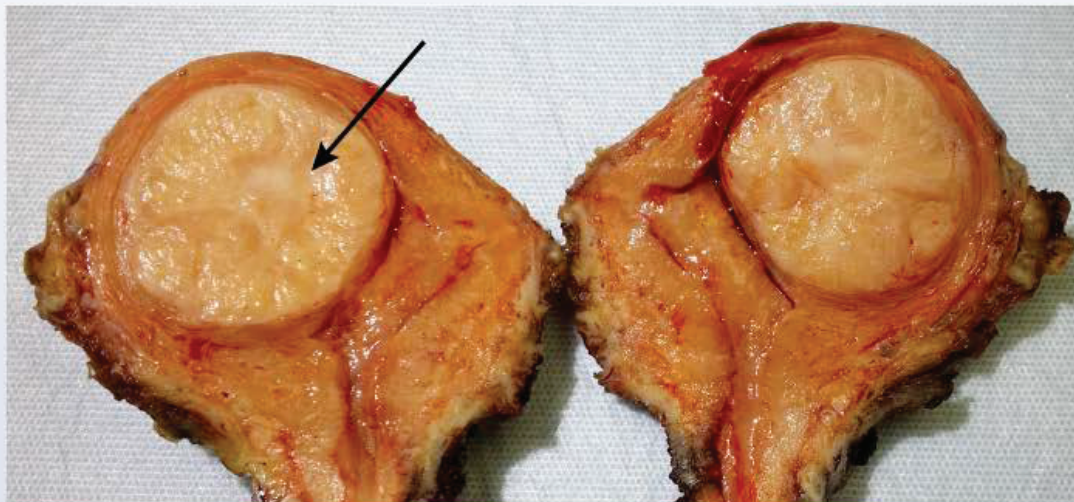
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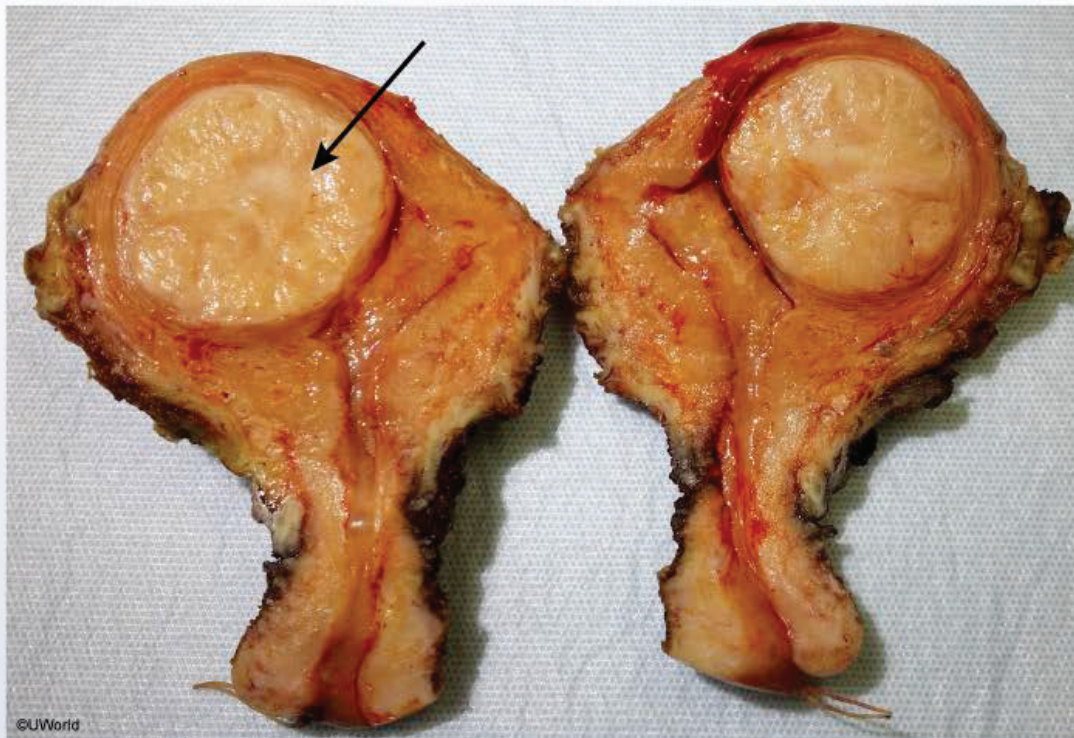


A 48-year-old woman comes to the office due to heavy menstrual bleeding for the last several months. The patient has monthly menses with 5-6 days of heavy bleeding and passage of large blood clots and increased abdominal cramping. She has no significant medical history and has had 2 vaginal deliveries. Her family history is significant for endometrial cancer in her mother. BMI is 24 kg/m<sup>2</sup>. Vital signs are normal. Pelvic ultrasound shows a uterine mass. The patient undergoes a total abdominal hysterectomy; gross examination of the uterus is shown below:





gross examination of the uterus is shown below:



The abnormal region indicated by the arrow is most likely to display which of the following microscopic





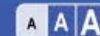


The abnormal region indicated by the arrow is most likely to display which of the following microscopic findings?

- ☐ A. Dysplastic squamocolumnar cells with areas of atypia
- ☐ B. Ectopic endometrial glands and hemosiderin-laden macrophages
- ☐ C. Hyperplastic proliferation of irregular endometrial glands
- ☐ D. Infiltration of the stroma by high-grade serous carcinoma
- ☐ E. Monoclonal proliferation of myocytes and fibroblasts

Submit





The abnormal region indicated by the arrow is most likely to display which of the following microscopic findings?

- ☐ A. Dysplastic squamocolumnar cells with areas of atypia (4%)
- ☐ B. Ectopic endometrial glands and hemosiderin-laden macrophages (3%)
- ☐ C. Hyperplastic proliferation of irregular endometrial glands (23%)
- ☐ D. Infiltration of the stroma by high-grade serous carcinoma (8%)
- ☒ E. Monoclonal proliferation of myocytes and fibroblasts (59%)

Correct

59%



01 min, 39 secs



10/11/2020

Block Time Remaining: 00:05:58

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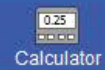
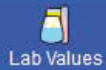
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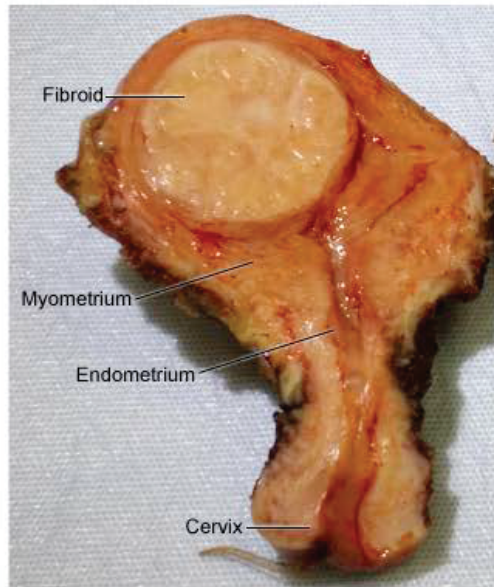
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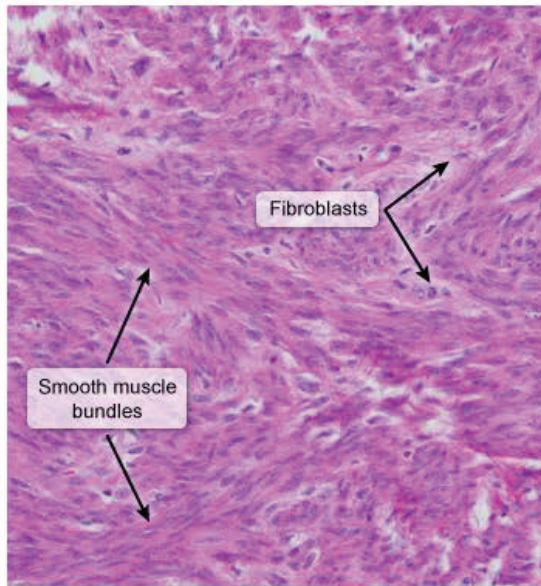
End Block



### Uterine leiomyoma (fibroids)



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This patient with heavy menses and a uterine mass has a **uterine leiomyoma**, also known as a fibroid.

**Fibroids** are common, benign tumors arising from smooth muscle cells and fibroblasts that can grow in a







This patient with heavy menses and a uterine mass has a **uterine leiomyoma**, also known as a fibroid.

**Fibroids** are common, benign tumors arising from smooth muscle cells and fibroblasts that can grow in a variety of sizes and locations within the uterine myometrium, resulting in variable clinical presentations.

This patient has an **intramural fibroid** (within the uterine wall), which can increase the endometrial surface area (due to mass effect) and result in **heavy menses**.

Patients with symptomatic uterine fibroids are often treated surgically with a hysterectomy. Grossly, fibroids appear as **discrete, yellow-gray tumors** with a thin pseudocapsule that separates the fibroid from the normal uterine myometrium. Diagnosis is confirmed with microscopy, which typically reveals **monoclonal proliferation of myocytes and fibroblasts** because each fibroid arises from a single progenitor smooth muscle cell. Due to their benign nature, fibroid myocytes are uniform in size and shape and have minimal mitotic figures.

**(Choice A)** Patients with cervical cancer are often asymptomatic or have irregular, postcoital spotting rather than heavy menses. **Cervical cancer** is typically found in the cervical transformation zone (rather than the uterine myometrium) and microscopy shows dysplastic squamocolumnar cells with areas of atypia.

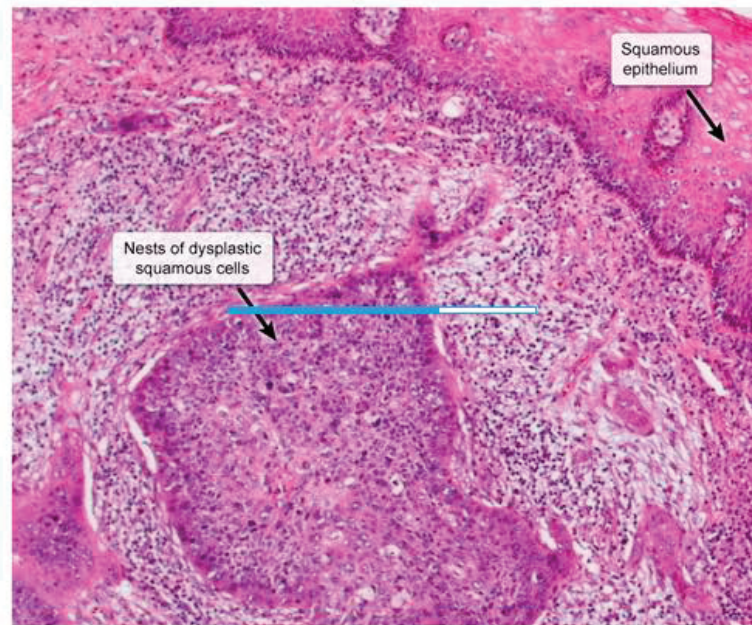
**(Choice B)** Patients with endometriosis typically present with painful menses (ie, dysmenorrhea); however,



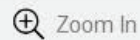


## Exhibit Display

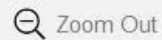
## Cervical squamous cell carcinoma



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(Choice B) Patients with endometriosis typically present with painful menses (ie, dysmenorrhea), however,







**(Choice B)** Patients with endometriosis typically present with painful menses (ie, dysmenorrhea); however, there are usually endometrial tissue implants **outside the uterus** rather than an intrauterine mass. Light microscopy typically reveals **ectopic endometrial glands** and hemosiderin-laden macrophages.

**(Choice C)** Patients with **endometrial hyperplasia** or cancer typically present with irregular, heavy menses and a thickened endometrium (rather than a mass in the myometrium). Histopathology typically reveals hyperplastic proliferation of irregular endometrial glands.

**(Choice D)** Microscopy of **ovarian cancer** typically reveals infiltration of the stroma by high-grade serous carcinoma. Ovarian cancer is unlikely in this patient as it typically causes an **adnexal mass** rather than a solitary intrauterine mass.

### Educational objective:

Uterine leiomyomas (ie, fibroids) are common, benign tumors arising from the uterine myometrium that occur due to monoclonal proliferation of myocytes and fibroblasts.

### References

- **Clonality of smooth muscle and fibroblast cell populations isolated from human fibroid and myometrial tissues.**



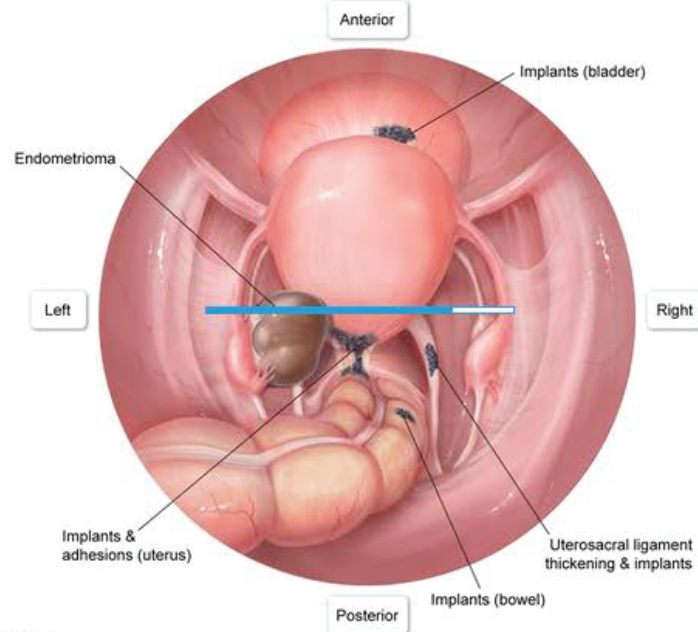




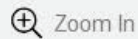
(Choice B) Patients with endometriosis typically present with painful menses (i.e., dysmenorrhea); however,

### Exhibit Display

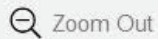
#### Pelvic endometriosis



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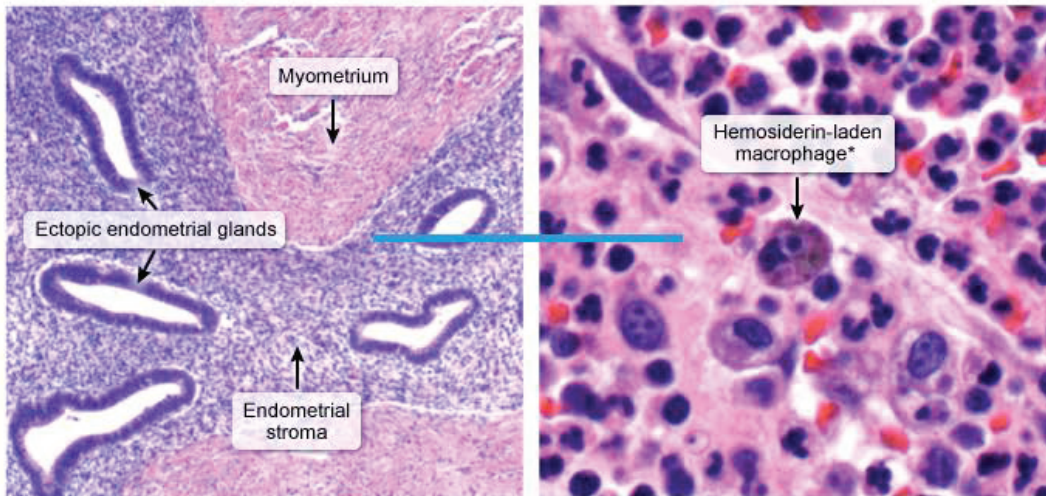




(Choice B) Patients with endometriosis typically present with painful menses (ie, dysmenorrhea); however,

### Exhibit Display

## Endometriosis



\*Breakdown of red blood cells (chronic bleeding)

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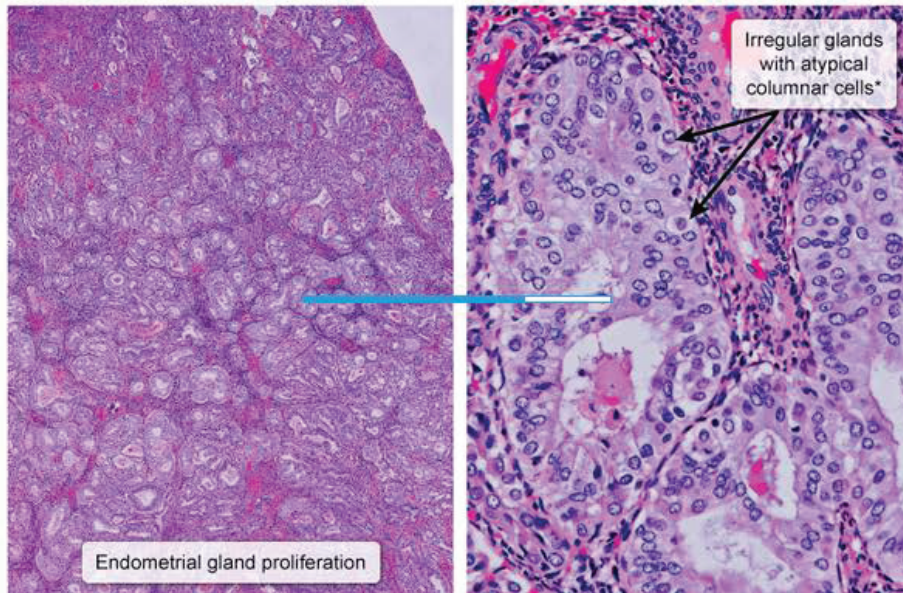




(Choice B) Patients with endometriosis typically present with painful menses (ie, dysmenorrhea); however,

### Exhibit Display

#### Atypical endometrial hyperplasia

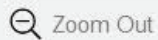


\*Loss of normal polarity; irregular, enlarged nuclei

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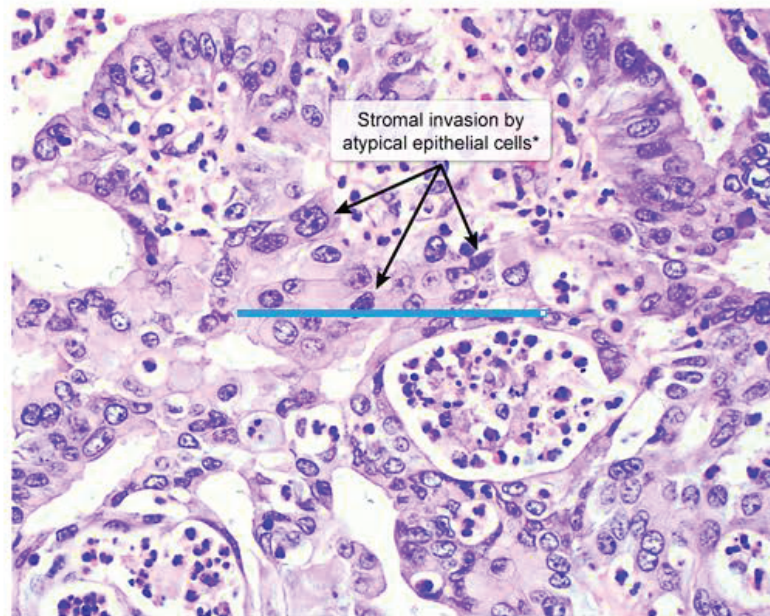




(Choice B) Patients with endometriosis typically present with painful menses (ie, dysmenorrhea); however,

### Exhibit Display

#### High-grade ovarian carcinoma



\*Hyperchromatic, pleomorphic nuclei (> 3x variation in size)

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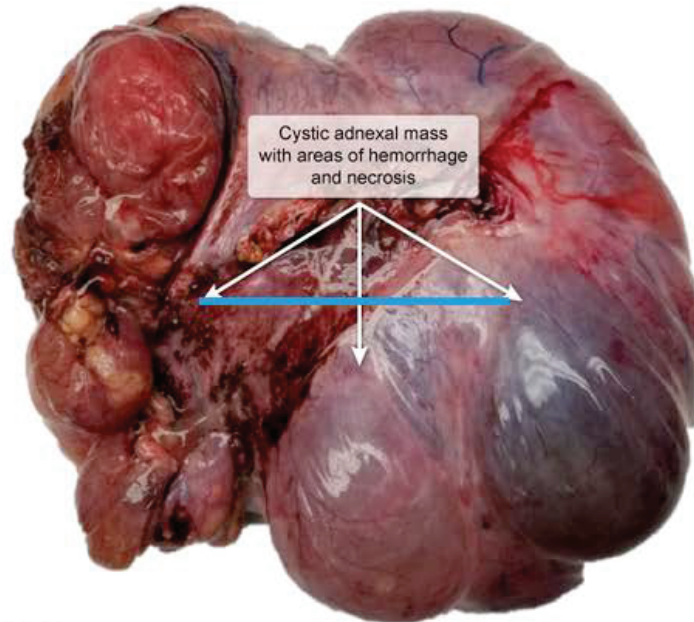
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(Choice B) Patients with endometriosis typically present with painful menses (ie, dysmenorrhea); however,

## Exhibit Display

## High-grade serous ovarian carcinoma



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A 47-year-old woman comes to the office with a red rash on her breast that has been present for approximately 2 months. The rash is itchy, and the skin feels rough to the touch. The itching has worsened in the past few weeks, and moisturizers have provided no relief. The patient has a history of surgery for bilateral silicone breast implants 10 years ago. Temperature is 37 C (98.6 F). Physical examination shows redness and swelling of the right breast without any discrete masses. The overlying skin is indurated with a dimpled texture, and several enlarged, hard lymph nodes are palpated in the right axilla. The left breast is normal. Which of the following is the most likely cause of this patient's skin changes?

- ☐ A. Deep venous thrombosis
- ☐ B. Foreign body reaction
- ☐ C. Infectious process
- ☐ D. Lymphatic obstruction
- ☐ E. Scar formation







approximately 2 months. The rash is itchy, and the skin feels rough to the touch. The itching has worsened in the past few weeks, and moisturizers have provided no relief. The patient has a history of surgery for bilateral silicone breast implants 10 years ago. Temperature is 37 C (98.6 F). Physical examination shows redness and swelling of the right breast without any discrete masses. The overlying skin is indurated with a **dimpled texture**, and several enlarged, hard lymph nodes are palpated in the right axilla. The left breast is normal. Which of the following is the most likely cause of this patient's skin changes?

- ☐ A. Deep venous thrombosis (0%)
- ☐ B. Foreign body reaction (19%)
- ☐ C. Infectious process (8%)
- ☒ D. Lymphatic obstruction (68%)
- ☐ E. Scar formation (3%)

Correct

68%



57 secs



01/30/2021

Block Time Remaining: 00:06:55

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Feedback



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End Block



Item 7 of 40

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Mark



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Lab Values



Notes



Calculator



Reverse Color



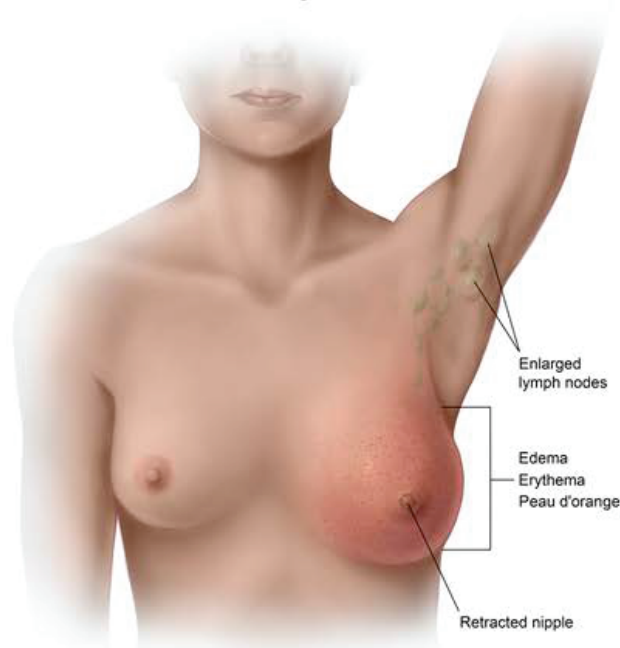
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### Exhibit Display

#### Inflammatory breast cancer



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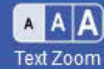
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End Block



This patient has a classic **peau d'orange** rash, which is characterized by a generalized, **erythematous** rash that may be tender or itchy. The skin texture is **firm** and **coarsely pitted** like an orange peel (after which it is named). This rapidly progressive dermatological finding (with or without an underlying mass) and **breast edema** are consistent with the characteristic presentation of **inflammatory breast cancer**, a poorly differentiated **breast malignancy** with an unfavorable prognosis.

The term "inflammatory" is a misnomer because the classic skin findings are not due to infection but are instead caused by cancerous cells **obstructing lymphatic drainage** after spreading to the dermal lymphatic spaces. Because of this cancer's propensity to metastasize to the lymphatic system, most patients have lymph node involvement (eg, **axillary lymphadenopathy**) at the time of presentation.

**(Choice A)** Deep venous thrombosis occurs due to hypercoagulability related to malignancy, surgery, or intravenous catheter placement. Deep venous thrombosis most often affects the lower extremities but can also involve the upper extremities. It presents with edema and pain in the affected limb.

**(Choice B)** Rupture of a silicone breast implant can lead to a foreign body reaction with local inflammation (eg, edema, induration), and granuloma formation can result in a palpable, tender mass. Although these findings can mimic inflammatory breast cancer, this patient's pitted skin texture (indicating lymphatic obstruction) and hard axillary lymph nodes make malignancy a more likely diagnosis.







## Exhibit Display

This patient has a rash that may be te which it is named).

and **breast edema** poorly differentiated

The term "inflamma instead caused by lymphatic spaces.

patients have lymph

**(Choice A)** Deep

intravenous cathete

also involve the up

**(Choice B)** Ruptur

(eg, edema, indura

findings can mimic

obstruction) and ha

Breast cancer classification		
	Diagnosis	Key features
Noninvasive	DCIS	<ul style="list-style-type: none"><li>Central necrosis</li><li>Precancerous lesion</li><li>Confined to ducts &amp; lobules</li></ul>
	Paget disease	<ul style="list-style-type: none"><li>Eczematous nipple lesion</li><li>Extension of DCIS into ducts</li></ul>
Invasive	Ductal carcinoma	<ul style="list-style-type: none"><li>Most common type</li><li>Nests &amp; cords of cells</li></ul>
	Lobular carcinoma	<ul style="list-style-type: none"><li>Small cells in single file</li><li>Mammary stroma invasion</li></ul>
	Inflammatory breast cancer	<ul style="list-style-type: none"><li>Peau d'orange</li><li>Dermal lymphatic invasion</li></ul>

DCIS = ductal carcinoma in situ.



New | Existing





(eg, edema, induration), and granuloma formation can result in a palpable, tender mass. Although these findings can mimic inflammatory breast cancer, this patient's pitted skin texture (indicating lymphatic obstruction) and hard axillary lymph nodes make malignancy a more likely diagnosis.

**(Choice C)** Mastitis (ie, breast infection) most commonly occurs in lactating women and presents with pain, breast swelling, and erythema. Most patients also have systemic findings such as fever, malaise, and leukocytosis.

**(Choice E)** Breast implant surgery requires surgical incisions that can leave scars on the breast skin. A **hypertrophic** scar is a thick, raised, and pink fibrous tissue line that follows the original incision. **Keloid** scars occur due to disorganized collagen deposits; they have a thick, rubbery appearance and extend outside the incision borders.

### Educational objective:

Peau d'orange is an erythematous, itchy breast rash with skin texture changes that resemble an orange peel. It is the key dermatologic presentation of inflammatory breast cancer and is caused by cancerous cells spreading to the dermal lymphatic spaces and obstructing lymphatic drainage.

### References

- [Inflammatory breast cancer: an overview.](#)





Item 7 of 40

Question Id: 1877



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

(eg. edema, induration), and granule formation can result in a palpable, tender mass. Although these

## Exhibit Display



Zoom In



Zoom Out



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New | Existing



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Feedback



Suspend



End Block





A 22-year-old woman presents to clinic for a medical check-up. She has been diagnosed with Turner's syndrome. Cardiovascular examination reveals no abnormalities of the heart or aorta. She asks about her chances of having a baby. Which of the following methods could be used to achieve pregnancy in this patient?

- ☐ A. Bromocriptine therapy
- ☐ B. Clomiphene citrate
- ☐ C. Pulsatile GnRH infusion
- ☐ D. hCG therapy
- ☐ E. In vitro fertilization (IVF)

Submit







A 22-year-old woman presents to clinic for a medical check-up. She has been diagnosed with Turner's syndrome. Cardiovascular examination reveals no abnormalities of the heart or aorta. She asks about her chances of having a baby. Which of the following methods could be used to achieve pregnancy in this patient?

- ☐ A. Bromocriptine therapy (0%)
- ☐ B. Clomiphene citrate (5%)
- ☐ C. Pulsatile GnRH infusion (12%)
- ☐ D. hCG therapy (1%)
- ☒ E. In vitro fertilization (IVF) (79%)

Correct

 79%  
Answered correctly

 29 secs  
Time Spent

 09/02/2020  
Last Updated

Explanation

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Most women with Turner syndrome (45,XO) are infertile secondary to ovarian failure. With sufficient estrogen and progestin supplementation, however, these women can develop a thick endometrial lining that is substantial enough to support a pregnancy. In vitro fertilization of Turner syndrome patients with an ovum provided by a related or anonymous donor results in pregnancy rates approaching 60%. A thorough renal, cardiac and thyroid examination should be carried out before pregnancy is attempted to reduce the potential for complications during pregnancy. Pregnancy can occur spontaneously in some patients with Turner syndrome, but the risk of spontaneous abortion, Down syndrome and Turner syndrome are all increased in such cases.

**(Choice A)** Bromocriptine is a dopamine receptor agonist that inhibits pituitary prolactin secretion. It can restore fertility in women with hyperprolactinemia.

**(Choice B)** Clomiphene citrate is an antiestrogen that stimulates ovulation by blocking the feedback inhibition of estrogen on the hypothalamus thereby enhancing the release of pituitary gonadotropins. It is best used to achieve fertility in women with ovulatory failure who are normogonadotropic, normoprolactinemic and euthyroid.







**(Choice C)** Pulsatile GnRH infusion can stimulate ovulation in women who have disordered hypothalamic GnRH secretion resulting in hypogonadotropic, hypogonadal anovulation. Pituitary and ovarian function must be intact for this method to work.

**(Choice D)** hCG therapy can be used to trigger the ovulatory cascade in an oocyte donor when her follicles are deemed mature.

### Educational objective:

In vitro fertilization using a donated ovum is the most promising means of achieving pregnancy in a woman with Turner syndrome. Pregnancy can occasionally occur spontaneously in some patients with Turner syndrome, but the risk of spontaneous abortion, Down syndrome and Turner syndrome are all increased in such cases.

Genetics

Subject

Female Reproductive System & Breast

System

Turner syndrome

Topic

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A newborn girl is evaluated in the nursery after an uncomplicated spontaneous vaginal delivery to a 29-year-old primigravida. The mother declined prenatal testing and ultrasound examination during the pregnancy. Her pregnancy was otherwise uneventful, and she took prenatal vitamins throughout. Examination of the neonate shows a posterior neck mass and bilateral nonpitting edema of the hands and feet. Femoral pulses are diminished. Neck ultrasound reveals a mass composed of cystic spaces separated by connective tissue. Which of the following is the most likely underlying mechanism responsible for this patient's condition?

- ☐ A. 21-hydroxylase deficiency
- ☐ B. Androgen receptor mutation
- ☐ C. Loss of paternal chromosome X
- ☐ D. Meiotic nondisjunction of fetal chromosome 18
- ☒ E. Partial deletion of the short arm of chromosome 5
- ☐ F. Robertsonian translocation involving fetal chromosome 21

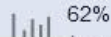




year-old primigravida. The mother declined prenatal testing and ultrasound examination during the pregnancy. Her pregnancy was otherwise uneventful, and she took prenatal vitamins throughout. Examination of the neonate shows a **posterior neck mass** and bilateral nonpitting edema of the hands and feet. Femoral pulses are diminished. Neck ultrasound reveals a mass composed of cystic spaces separated by connective tissue. Which of the following is the most likely underlying mechanism responsible for this patient's condition?

- ☐ A. 21-hydroxylase deficiency (3%)
- ☐ B. Androgen receptor mutation (1%)
- ☒ C. Loss of paternal chromosome X (62%)
- ☐ D. Meiotic nondisjunction of fetal chromosome 18 (11%)
- ☐ E. Partial deletion of the short arm of chromosome 5 (12%)
- ☐ F. Robertsonian translocation involving fetal chromosome 21 (9%)

Correct



62%

Answered correctly



01 min, 18 secs

Time Spent



10/10/2020

Last Updated

Block Time Remaining: 00:08:42

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Item 9 of 40

Question Id: 339



Mark

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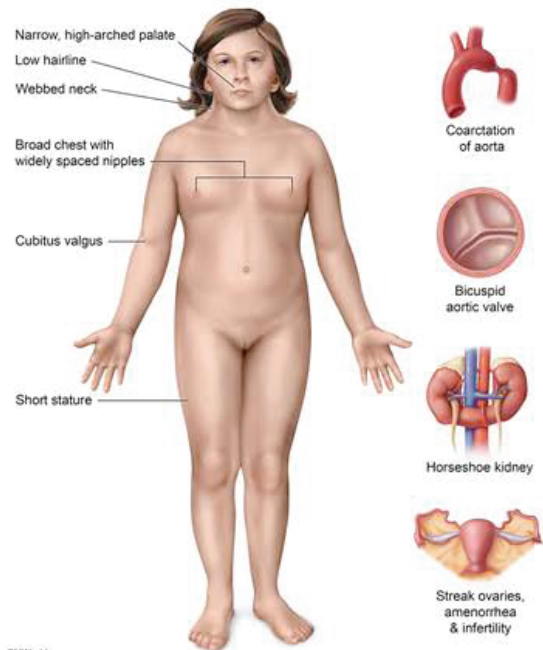
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### Exhibit Display

#### Turner syndrome



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This patient's posterior neck mass is most likely a **cystic hygroma**, and the bilateral extremity swelling is consistent with **lymphedema**. These findings in the context of **diminished femoral pulses** (suggestive of **coarctation of the aorta**) in a newborn girl are classic for Turner syndrome. Turner syndrome is characterized by a 45,X karyotype due to **loss of paternal chromosome X**. Both cystic hygromas and lymphedema occur due to abnormalities of lymphatic outflow in Turner syndrome. The swelling decreases with age.

**(Choice A)** In congenital adrenal hyperplasia (adrenogenital syndrome), patients have abnormal sexual differentiation due to defective hormone synthesis in the adrenal glands. The most common enzymatic defect is 21-hydroxylase deficiency. At birth, patients have ambiguous genitalia (girls only) and salt wasting (hypotension, hyponatremia).

**(Choice B)** Androgen insensitivity syndrome results from a defect in testosterone receptors. The typical presentation is a 46,XY adolescent who appears phenotypically female but has primary amenorrhea due to the absence of an internal female reproductive tract and the presence of cryptorchid testes.

**(Choice D)** Trisomy 18 (Edward syndrome) is usually caused by meiotic nondisjunction. These patients have multiple anomalies, including cardiac defects, clenched fists, rocker bottom feet, omphalocele, and





the absence of an internal female reproductive tract and the presence of cryptorchid testes.

**(Choice D)** Trisomy 18 (Edward syndrome) is usually caused by meiotic nondisjunction. These patients have multiple anomalies, including cardiac defects, clenched fists, rocker bottom feet, omphalocele, and low-set ears.

**(Choice E)** *Cri du chat* is most commonly due to a de novo partial deletion of the short arm of chromosome 5 (5p-). Patients with *cri du chat* syndrome typically have a round face, catlike cry, and microcephaly.

**(Choice F)** Down syndrome (DS) results from meiotic nondisjunction or Robertsonian translocation involving fetal chromosome 21. These patients have a flat face, oblique palpebral fissures, and epicanthal folds. Atrioventricular defects are the most common cardiac anomaly. Although cystic hygromas can occur in patients with DS, the absence of the dysmorphic features of DS makes this diagnosis unlikely.

### Educational objective:

Turner syndrome (45,X) manifests in the neonate with lymphedema and cystic hygromas. Short stature, primary amenorrhea, and aortic anomalies are the other important clinical features.

### References

- [Turner syndrome: diagnosis and management.](#)







A 16-year-old girl comes to the office due to pelvic and crampy lower abdominal pain that seems to recur at the beginning of each month and resolves after a day or two. She thinks the pain began approximately 6 months ago, and it is worsening significantly each month. The patient has never had a menstrual period. She and her boyfriend have not had any form of sexual intercourse, including digital, oral, vaginal, or anal. The patient's weight, height, and BMI are average for age and sex, and she has fully developed secondary sexual characteristics. Examination reveals a palpable mass anterior to the rectum. Serum  $\beta$ -hCG is negative. Which of the following is the most likely diagnosis in this patient?

- ☐ A. Androgen insensitivity syndrome
- ☐ B. Asherman syndrome
- ☐ C. Endometriosis
- ☐ D. Imperforate hymen
- ☐ E. Kallmann syndrome
- ☐ F. Turner syndrome





the beginning of each month and resolves after a day or two. She thinks the pain began approximately 6 months ago, and it is worsening significantly **each month**. The patient has never had a menstrual period. She and her boyfriend have not had any form of sexual intercourse, including digital, oral, vaginal, or anal. The patient's weight, height, and BMI are average for age and sex, and she has fully developed secondary sexual characteristics. Examination reveals a palpable mass anterior to the rectum. Serum  $\beta$ -hCG is negative. Which of the following is the most likely diagnosis in this patient?

- ☐ A. Androgen insensitivity syndrome (8%)
- ☐ B. Asherman syndrome (5%)
- ☐ C. Endometriosis (20%)
- ☒ D. Imperforate hymen (61%)
- ☐ E. Kallmann syndrome (3%)
- ☐ F. Turner syndrome (1%)

Correct

61%

48 secs

09/30/2020





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



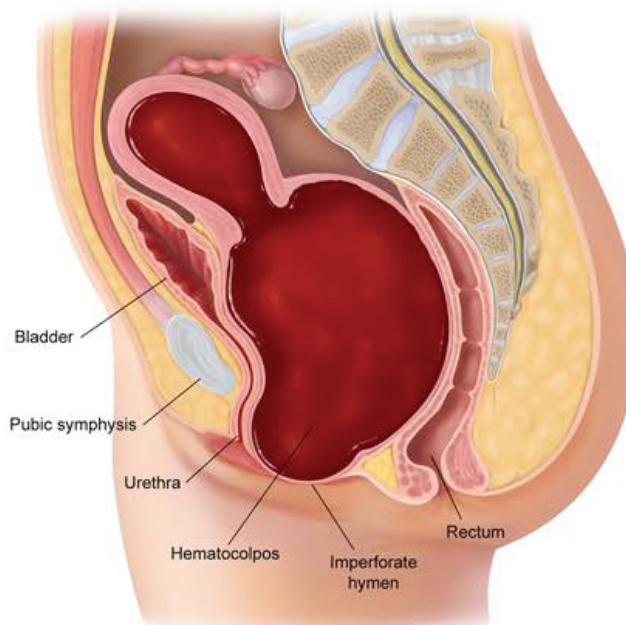
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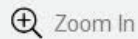
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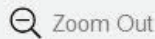
#### Hematocolpos



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Zoom In



Zoom Out



Reset



New



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My Notebook

My Notebook



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Feedback



Suspend



End Block





An **imperforate hymen** is an obstructive lesion caused by incomplete degeneration of the central portion of the fibrous tissue band connecting the walls of the vagina. At birth, vaginal secretions stimulated by the mother's estrogen can cause mucocolpos (accumulation of mucus in the vaginal canal), which may manifest as a bulging introitus. If the condition remains undiagnosed, the mucus is reabsorbed and the child will be asymptomatic until menarche. The patient may then present with **primary amenorrhea** and normal secondary sexual characteristics with **cyclic** abdominal or **pelvic pain** due to accumulation of menstrual blood in the vagina and uterus (eg, **hematocolpos**). The pressure from the resulting collection of blood can also cause back pain and difficulties with defecation. **Secondary sexual development** is normal as the patient has no chromosomal or hormonal abnormalities. Examination may show a **vaginal bulge** and/or mass palpated anterior to the rectum.

**(Choice A)** Patients with **androgen insensitivity syndrome** are genetically male but have a female phenotype due to resistance to testosterone. In adolescence, breast development results from peripheral conversion of testosterone to estrogen, but axillary and pubic hair is absent. Primary amenorrhea occurs due to a complete absence of Müllerian structures.

**(Choice B)** Asherman syndrome causes secondary amenorrhea through obstruction from scarring of the uterine cavity. This is typically a sequela of uterine infection (eg, postpartum endometritis) or procedures (eg, dilation and curettage).





Item 10 of 40

Question Id: 8390



Mark



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Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



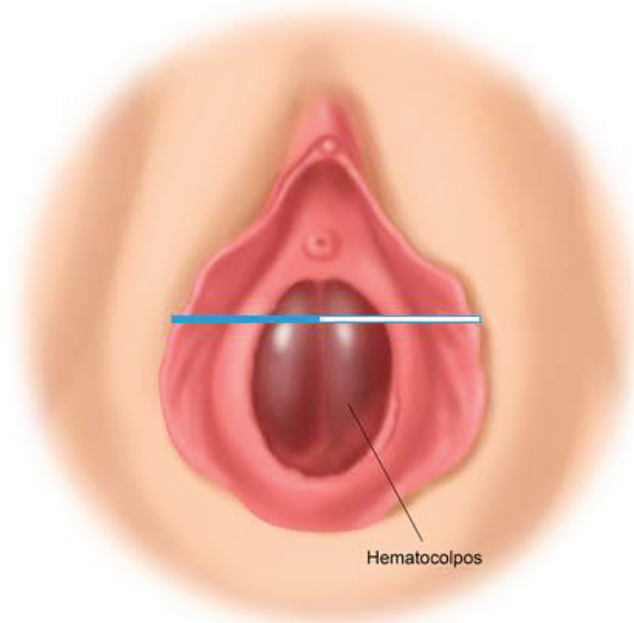
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### Exhibit Display

#### Imperforate hymen



Hematocolpos

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Block Time Remaining: 00:09:30

TUTOR

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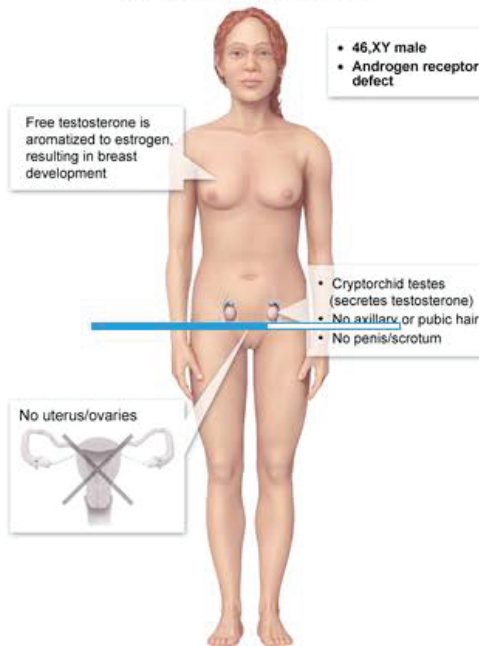


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## Exhibit Display

## Androgen insensitivity syndrome



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**(Choice B)** Asherman syndrome causes secondary amenorrhea through obstruction from scarring of the uterine cavity. This is typically a sequela of uterine infection (eg, postpartum endometritis) or procedures (eg, dilation and curettage).

**(Choice C)** **Endometriosis** is the presence of endometrial glands and stroma outside the uterus. It may cause severe dysmenorrhea (not amenorrhea) with lower abdominal cramps that begin 1-2 days before menses. A common site of endometrial implants is the pouch of Douglas, which presents as painful defecation, dyspareunia, and palpable nodularity on rectovaginal examination.

**(Choice E)** **Kallmann syndrome** occurs due to impaired synthesis of gonadotropin-releasing hormone by the hypothalamus. The condition presents with primary amenorrhea, absent secondary sexual characteristics, and an olfactory sensory defect.

**(Choice F)** Turner syndrome (45,XO) is the most common cause of primary amenorrhea. Affected individuals have short stature, webbed neck, shielded chest, and fibrotic ovaries, and do not develop secondary sexual characteristics.

### Educational objective:

Imperforate hymen is caused by incomplete degeneration of the central portion of the fibrous tissue band connecting the walls of the vagina. Adolescent patients typically present with primary amenorrhea, normal





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



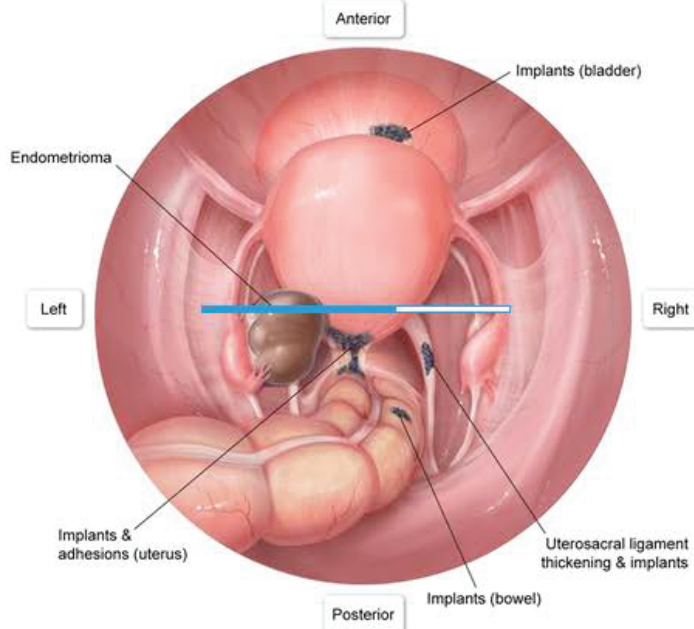
Text Zoom



Settings

### Exhibit Display

#### Pelvic endometriosis



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Zoom In



Zoom Out



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My Notebook

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TUTOR

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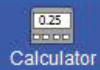
Feedback



Suspend

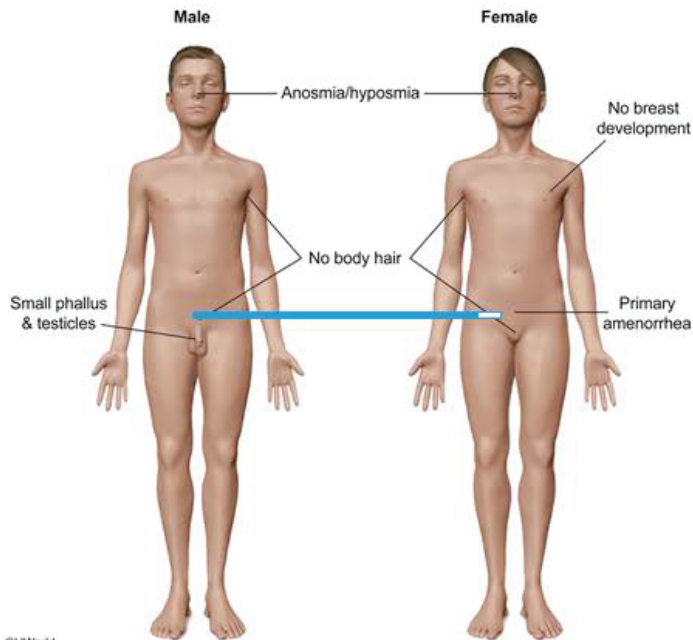


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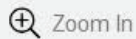


### Exhibit Display

#### Kallmann syndrome



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connecting the walls of the vagina. Adolescent patients typically present with primary amenorrhea, normal







menstrual. A common site of endometrial implants is the pouch of Douglas, which presents as painful

defecation, dyspareunia, and palpable nodularity on rectovaginal examination.

**(Choice E)** [Kallmann syndrome](#) occurs due to impaired synthesis of gonadotropin-releasing hormone by the hypothalamus. The condition presents with primary amenorrhea, absent secondary sexual characteristics, and an olfactory sensory defect.

**(Choice F)** Turner syndrome (45,XO) is the most common cause of primary amenorrhea. Affected individuals have short stature, webbed neck, shielded chest, and fibrotic ovaries, and do not develop secondary sexual characteristics.

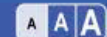
### Educational objective:

Imperforate hymen is caused by incomplete degeneration of the central portion of the fibrous tissue band connecting the walls of the vagina. Adolescent patients typically present with primary amenorrhea, normal secondary sexual characteristics, and cyclic abdominal or pelvic pain due to accumulation of menstrual blood in the vagina and uterus (eg, hematocolpos).

### References

- [Committee opinion: no. 562: Müllerian agenesis: diagnosis, management, and treatment.](#)
- [The presentation and management of complex female genital malformations.](#)





A 27-year-old woman, gravida 3 para 0 aborta 3, comes to the office for evaluation of fertility difficulties. The patient was started on combined oral contraceptive pills at age 22. She had no periods while using oral contraceptives and was advised that this was normal and of no concern. The patient stopped her contraception a year ago in an attempt to conceive with her husband but still has not menstruated. Her past medical history includes 3 elective first-trimester pregnancy terminations in her late teens. TSH, FSH, LH, prolactin, and quantitative  $\beta$ -hCG are normal. As part of the evaluation for amenorrhea, 10 days of oral medroxyprogesterone is administered. A few days after completing her progesterone course, the patient has moderately heavy bleeding with some cramping. Which of the following endometrial processes caused the bleeding?

- ☐ A. Apoptosis
- ☐ B. Dysplasia
- ☐ C. Granulation
- ☐ D. Hyperplasia
- ☐ E. Hypertrophy





oral contraceptives and was advised that this was normal and of no concern. The patient stopped her contraception a year ago in an attempt to conceive with her husband but still has not menstruated. Her past medical history includes 3 elective first-trimester pregnancy terminations in her late teens. TSH, FSH, LH, prolactin, and quantitative  $\beta$ -hCG are normal. As part of the evaluation for amenorrhea, 10 days of oral medroxyprogesterone is administered. A few days after completing her progesterone course, the patient has moderately heavy bleeding with some cramping. Which of the following endometrial processes caused the bleeding?

- ☒ A. Apoptosis (69%)
- ☐ B. Dysplasia (0%)
- ☐ C. Granulation (3%)
- ☐ D. Hyperplasia (19%)
- ☐ E. Hypertrophy (6%)

Correct

69%  
Answered correctly59 secs  
Time Spent02/13/2021  
Last Updated

Block Time Remaining: 00:10:30

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Feedback



Suspend



End Block





Item 11 of 40

Question Id: 299



Mark



Previous



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Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



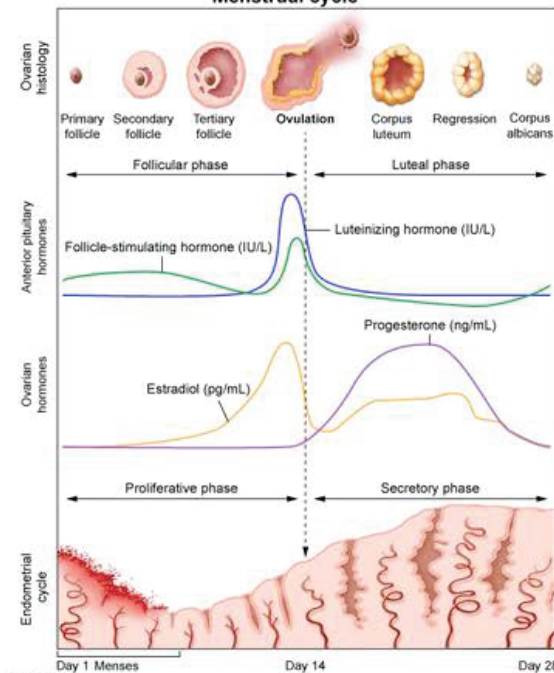
Text Zoom



Settings

## Exhibit Display

## Menstrual cycle



Zoom In

Zoom Out

Reset

New | Existing

My Notebook

Block Time Remaining: 00:10:30

TUTOR

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Feedback



Suspend



End Block



Progesterone is typically secreted in the luteal phase of the menstrual cycle and stimulates the endometrium to transform from proliferative to secretory to become a hospitable environment for embryonic implantation. Endometrial glands become more elaborate and the spiral arteries coil. Exogenous intake of progesterone for approximately 10 days similarly matures the endometrial lining.

When the endometrium is no longer exposed to progesterone (eg, in a **progesterone withdrawal test**), prostaglandin production increases, leading to **vasoconstriction of the spiral arteries**. Progesterone withdrawal also causes increased secretion of metalloproteases by endometrial stromal cells (causing degradation of the extracellular matrix) and **apoptosis** of the endometrial epithelium. The net effect is degeneration of the functionalis layer, which sloughs away as **menstrual flow**.

**(Choice B)** Dysplasia is the abnormal growth of cells, tissues, or organs. In epithelial tissues such as the transformation zone of the cervix, dysplasia is a very early form of precancer.

**(Choice C)** Granulation is a process of scar formation that involves deposition of connective tissue and angiogenesis. This patient's prior terminations put her at risk for Asherman syndrome and amenorrhea caused by post-procedural intrauterine scarring. Patients with Asherman syndrome do not experience progesterone withdrawal bleeding as the endometrium is essentially replaced with scar tissue.





**(Choice D)** Hyperplasia is the enlargement of tissue or an organ due to an increase in the number of cells. In the uterus, hyperplasia is frequently a precancerous state caused by excess estrogen exposure that stimulates endometrial proliferation. The progesterone in the patient's combined oral contraceptives and medroxyprogesterone would have suppressed endometrial proliferation.

**(Choice E)** Hypertrophy is an enlargement of tissue or an organ due to an increase in the size of its cells. Uterine hypertrophy is commonly seen in [adenomyosis](#).

### Educational objective:

Progesterone is the primary hormone responsible for stimulating the endometrium so that it is suitable for implantation. Progesterone withdrawal causes endometrial cells to undergo apoptosis, resulting in menstrual bleeding.

### References

- [Apoptosis in human endometrium and endometriosis](#).

Physiology

Subject

Female Reproductive System &amp; Breast

System

Apoptosis

Topic

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Item 11 of 40

Question Id: 299



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Lab Values

Notes

Calculator

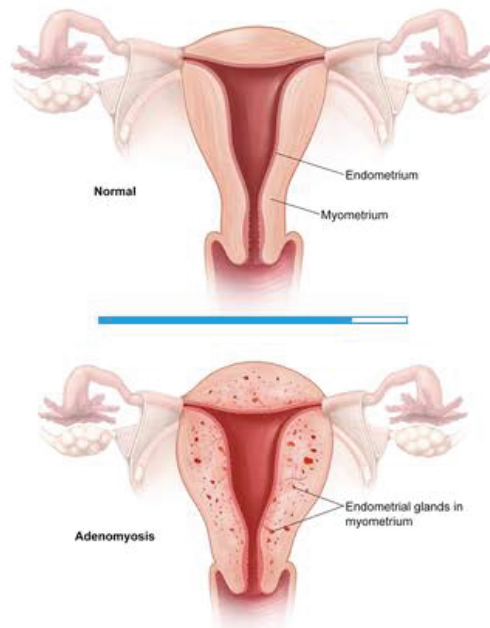
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Text Zoom

Settings

### Exhibit Display

Normal uterus vs adenomyosis



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Zoom In

Zoom Out

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Block Time Remaining: 00:10:30

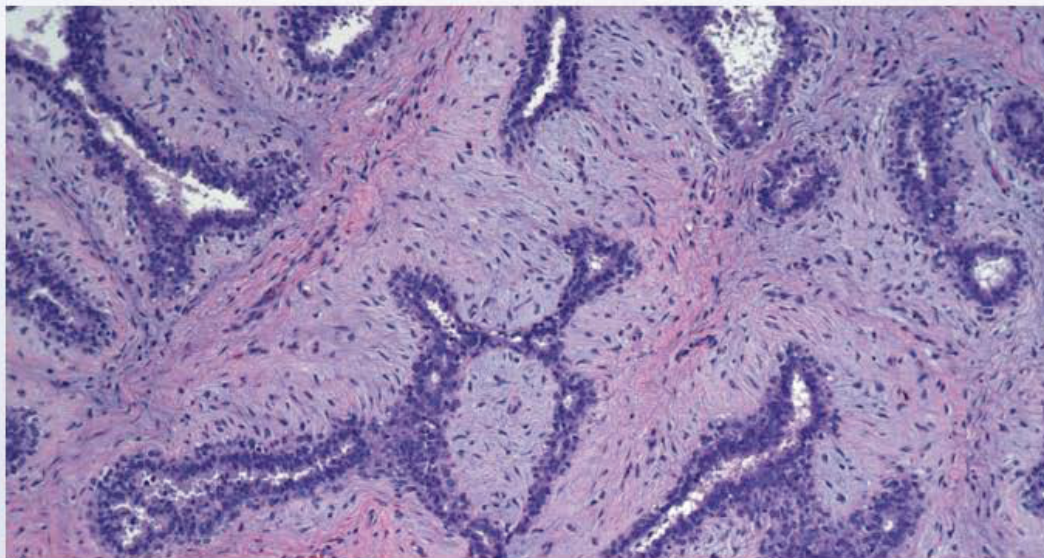
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A 34-year-old woman comes to the clinic due to a mass in her right breast. She discovered the mass after reading a magazine article recommending that women should perform breast self-examination regularly. The patient has no significant past medical history. A 2-cm nodule is noted on examination of the breast, and the patient is referred for biopsy. Histologic evaluation of the tissue specimen is shown in the image below.





Mark



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Full Screen



Tutorial



Lab Values



Notes



Calculator



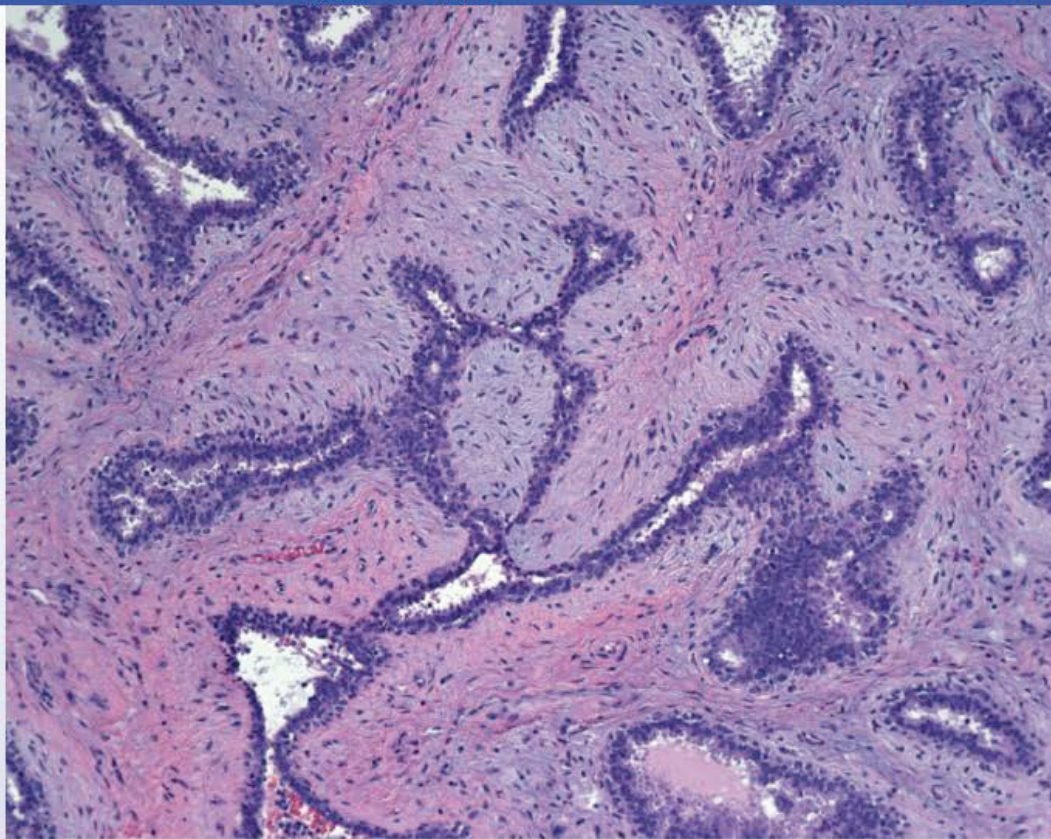
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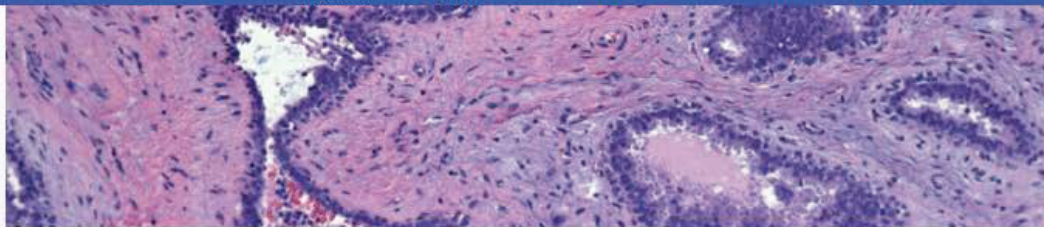


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End Block





Which of the following is the most likely diagnosis?

- ☐ A. Ductal carcinoma in situ
- ☐ B. Fibroadenoma
- ☐ C. Mammary duct ectasia
- ☐ D. Medullary carcinoma
- ☐ E. Paget disease
- ☐ F. Sclerosing adenosis

Submit





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



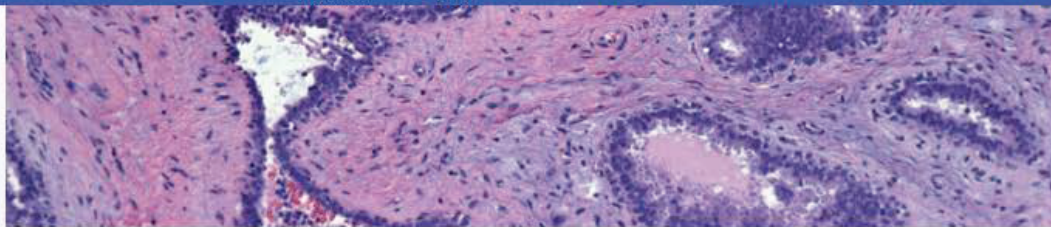
Reverse Color



Text Zoom



Settings



Which of the following is the most likely diagnosis?

- ☐ A. Ductal carcinoma in situ (14%)
- ☒ B. Fibroadenoma (67%)
- ☐ C. Mammary duct ectasia (3%)
- ☐ D. Medullary carcinoma (3%)
- ☐ E. Paget disease (1%)
- ☐ F. Sclerosing adenosis (9%)

Correct

67%  
Answered correctly

01 min, 21 secs  
Time Spent

02/04/2021  
Last Updated



Feedback



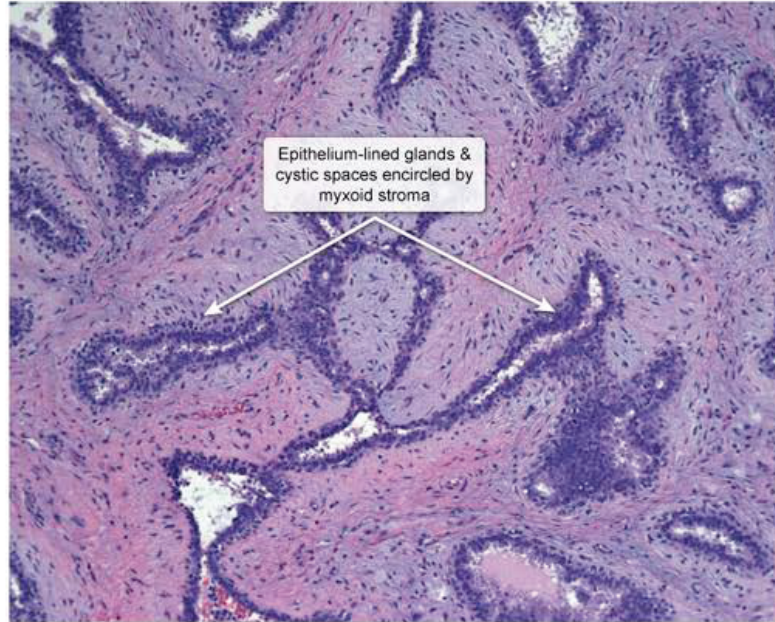
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End Block

### Exhibit Display

#### Fibroadenoma



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**Fibroadenoma** is the most common benign tumor of the breast, typically arising in young women age 15-35. Fibroadenomas are characterized by nodules that are well-demarcated, painless, mobile, and spherical and can be 1-10 cm in size. They can also occur as multiple and/or bilateral lesions. In younger women, fibroadenomas are usually discovered as a palpable mass by the patient or physician; in older patients, they are more often found incidentally on mammography. They often increase in size during pregnancy, lactation, or with estrogen therapy and usually regress after menopause.

Histologically, fibroadenomas are characterized by a benign-appearing cellular or **myxoid stroma** that encircles epithelium-lined glandular and cystic spaces (arrow). The lesions have a well-defined border but may compress and distort the surrounding glandular epithelium. As women age, the epithelium atrophies and the stroma becomes more hyalinized.

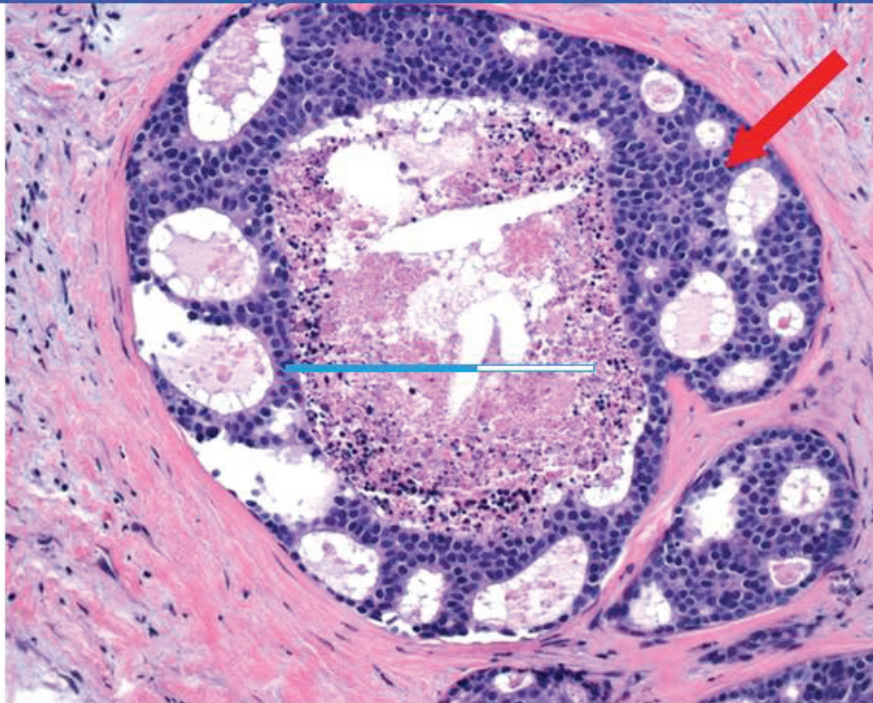
**(Choice A)** **Ductal carcinoma in situ (DCIS)** is a breast lesion characterized by a malignant clonal cell proliferation contained by the surrounding ductal basement membrane. The (basal) myoepithelial layer of the duct is preserved and uninvolved.

**(Choice C)** Mammary duct ectasia is characterized by ductal dilation, inspissated breast secretions, and chronic granulomatous inflammation in the periductal and interstitial areas.





## Exhibit Display



Zoom In



Zoom Out



Reset



New | Existing



My Notebook

Chronic granulomatous inflammation in the periductal and interstitial areas.







the duct is preserved and uninvolved.

**(Choice C)** Mammary duct ectasia is characterized by ductal dilation, inspissated breast secretions, and chronic granulomatous inflammation in the periductal and interstitial areas.

**(Choice D)** [Medullary carcinoma](#) is characterized by solid sheets of vesicular, pleomorphic, mitotically active cells with a significant lymphoplasmacytic infiltrate around and within the tumor and a pushing, noninfiltrating border.

**(Choice E)** [Paget disease of the nipple](#) is a rare form of breast cancer in which malignant cells spread from superficial DCIS into nipple skin without crossing the basement membrane. Physical examination shows unilateral erythema and scale crust around the nipple.

**(Choice F)** [Sclerosing adenosis](#) is characterized by central acinar proliferation and compression with surrounding fibrotic tissue and peripheral ductal dilation. Sclerosing adenosis is a common finding in fibrocystic change.

### Educational objective:

Fibroadenomas are the most common benign tumor of the breast. They are characterized histologically by a cellular or myxoid stroma that encircles and sometimes compresses epithelium-lined glandular and cystic spaces.





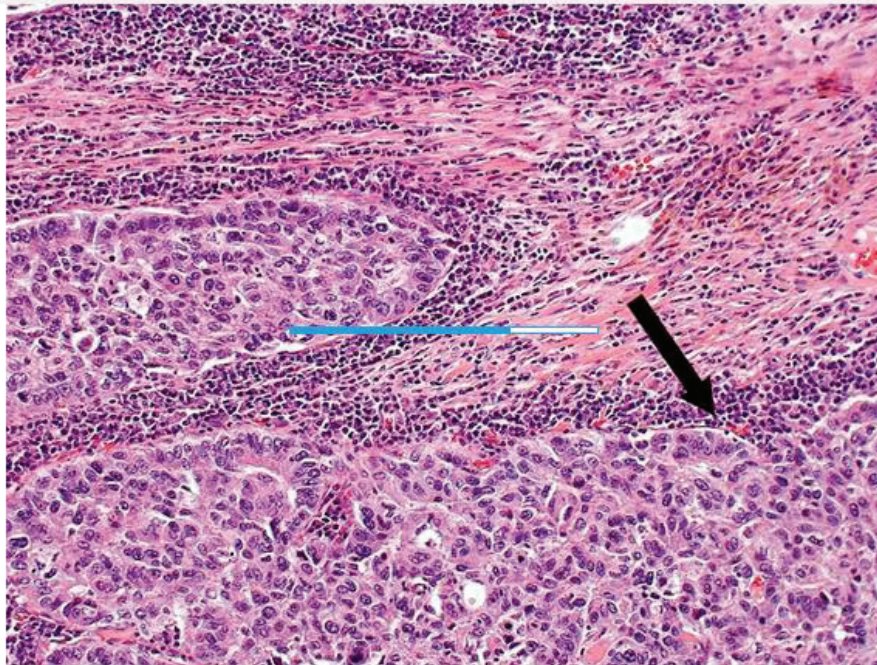


the duct is preserved and uninvolved.

### Exhibit Display

Medullary carcinoma of the breast

Medullary carcinoma of the breast



Zoom In



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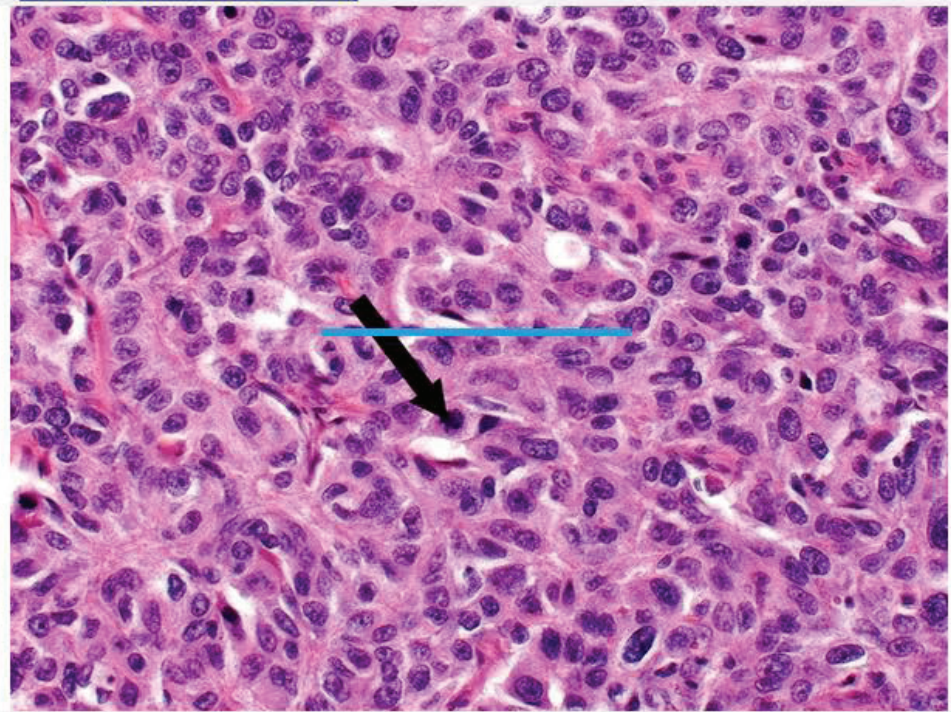
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the duct is preserved and uninvolved.

Exhibit Display

Medullary carcinoma of the breast Medullary carcinoma of the breast



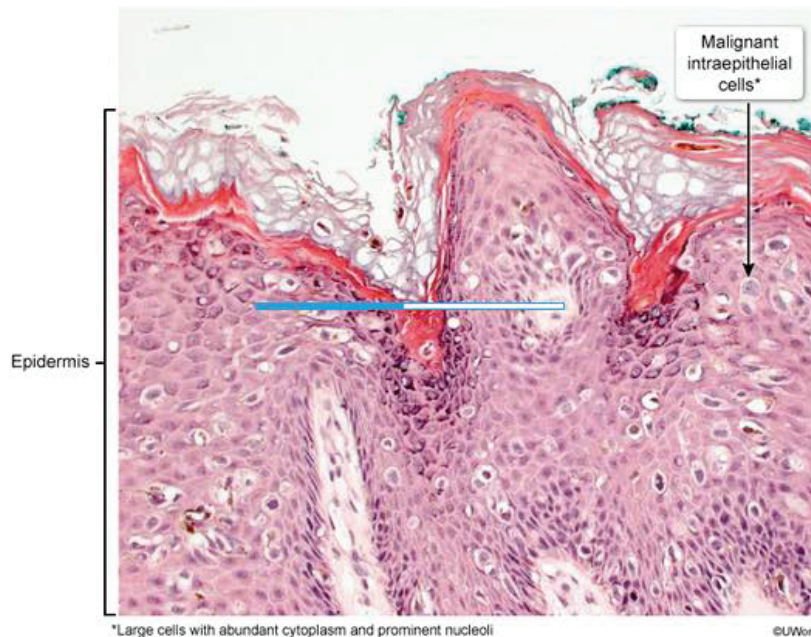




the duct is preserved and uninvolved.

### Exhibit Display

#### Paget disease of the breast



Zoom In

Zoom Out

Reset

New | Existing

My Notebook







Item 12 of 40

Question Id: 1109



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



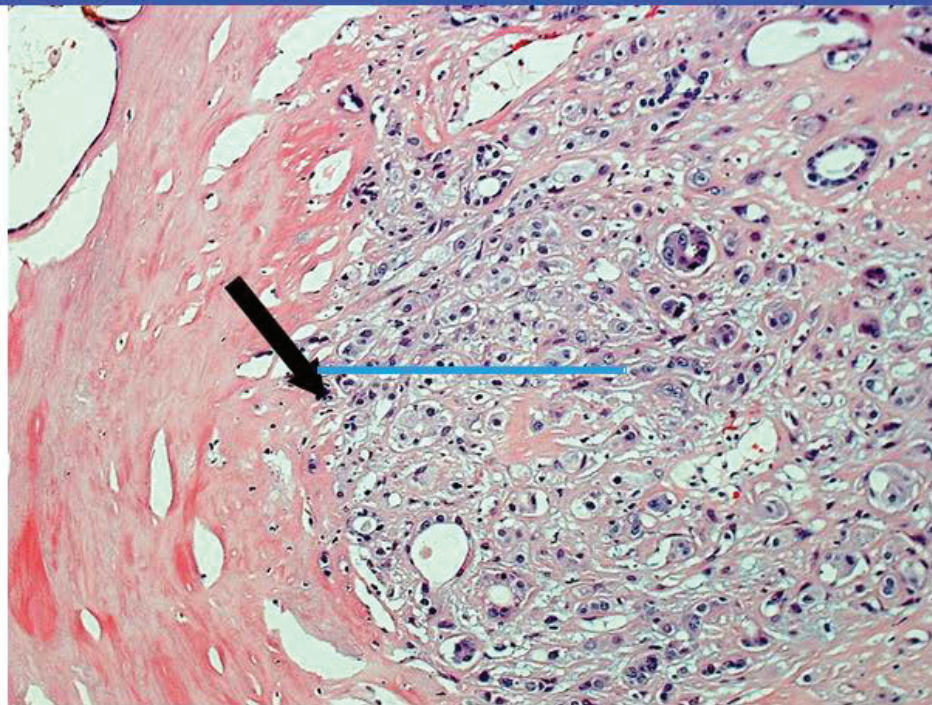
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Settings

the duct is preserved and uninvolved.

### Exhibit Display



Zoom In

Zoom Out

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My Notebook

Block Time Remaining: 00:11:51

TUTOR

<https://t.me/USMLEWorldStep1>



1



Feedback



Suspend



End Block



A 60-year-old woman, gravida 1, para 1, comes to the office with abdominal distension and decreased appetite. She also has lost 10 pounds (4.5 kg) unintentionally over the past few months. She takes no medications and has received all recommended vaccinations except for the human papilloma vaccine. The patient's mother had *BRCA*-positive ovarian cancer and died at the age of 55. BMI is 30kg/m<sup>2</sup>. Imaging studies reveal a right-sided ovarian mass and an accumulation of free peritoneal fluid. Her blood work shows a marked elevation of CA-125. Which of the following most likely would have reduced the risk of this patient's condition?

- ☐ A. Consistent condom use
- ☐ B. Long-term antioxidant supplementation
- ☐ C. Nulliparity
- ☐ D. Use of oral contraceptives
- ☐ E. Vaccination

**Submit**

Block Time Remaining: 00:11:52

TUTOR

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1



Feedback



Suspend



End Block



A 60-year-old woman, gravida 1, para 1, comes to the office with abdominal distension and decreased appetite. She also has lost 10 pounds (4.5 kg) unintentionally over the past few months. She takes no medications and has received all recommended vaccinations except for the human papilloma vaccine. The patient's mother had *BRCA*-positive ovarian cancer and died at the age of 55. BMI is 30kg/m<sup>2</sup>. Imaging studies reveal a right-sided ovarian mass and an accumulation of free peritoneal fluid. Her blood work shows a marked elevation of CA-125. Which of the following most likely would have reduced the risk of this patient's condition?

- ☐ A. Consistent condom use (3%)
- ☐ B. Long-term antioxidant supplementation (10%)
- ☐ C. Nulliparity (8%)
- ☒ D. Use of oral contraceptives (70%)
- ☐ E. Vaccination (7%)







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

### Epithelial ovarian cancer

#### Risk factors

- Family history
- Infertility
- Nulliparity
- Polycystic ovarian syndrome
- Endometriosis
- *BRCA1* or *BRCA2* mutations
- Lynch syndrome
- Postmenopausal hormone therapy

#### Protective factors

- Combined oral contraceptives
- Multiparity
- Breastfeeding
- Salpingo-oophorectomy

This patient's presentation is most likely due to **epithelial ovarian cancer (EOC)**. Common manifestations include abdominal distension, ascites, pleural effusion, bowel obstruction, decreased appetite, weight loss.



1



Feedback



Suspend



End Block



### • Salpingo-oophorectomy

This patient's presentation is most likely due to **epithelial ovarian cancer (EOC)**. Common manifestations include abdominal distension, ascites, pleural effusion, bowel obstruction, decreased appetite, weight loss, and an ovarian mass. Patients with EOC often present with advanced disease and increased mortality risk due to the lack of effective screening methods. **Cancer antigen 125 (CA-125)** is a protein produced by ovarian epithelia and is usually markedly elevated in cancerous ovarian cells compared to normal cells. However, CA-125 is neither sensitive nor specific for early EOC as it can be found in normal tissue and other cancers.

Women with **BRCA mutations** are at significantly increased risk for ovarian cancer. Additional **risk factors** include repeated ovulation, such as nulliparity (**Choice C**) or ovarian dysfunction (eg, infertility). These conditions inflict minor trauma to the ovarian surface, therefore rendering the epithelia susceptible to transformation.

**Protective factors** include **oral contraceptives**, multiparity, and breastfeeding. The common mechanism of these protective factors is less repair at the ovarian surface due to reduced lifetime ovulation frequency.

**(Choices A and E)** Consistent condom use and the human papilloma virus (HPV) vaccine can reduce transmission of high-risk HPV, which in turn can reduce the risk of cervical, vaginal, and vulvar cancer in





**Protective factors** include **oral contraceptives**, multiparity, and breastfeeding. The common mechanism of these protective factors is less repair at the ovarian surface due to reduced lifetime ovulation frequency.

**(Choices A and E)** Consistent condom use and the human papilloma virus (HPV) vaccine can reduce transmission of high-risk HPV, which in turn can reduce the risk of cervical, vaginal, and vulvar cancer in women. HPV infection is not linked to ovarian cancer.

**(Choice B)** Antioxidants neutralize reactive oxygen species and free radicals, thereby decreasing their damage to cells. However, long-term antioxidant supplementation (eg, vitamin C) has not been proven to decrease the risk of any cancer, including ovarian cancer.

### Educational objective:

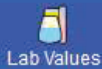
The pathogenesis of epithelial ovarian cancer is linked to the frequency of trauma and repair at the ovarian surface. Oral contraceptives, multiparity, and breastfeeding are protective by decreasing the frequency of ovulation. Risk factors include *BRCA* mutation, nulliparity, and infertility.

### References

- [ACOG Practice Bulletin No. 89. Elective and risk reducing salpingo-oophorectomy](#)
- [Hormone prevention strategies for breast, endometrial and ovarian cancers.](#)







A 15-year-old girl is brought in for evaluation of amenorrhea. She has never menstruated, but her mother had menarche at age 14. The patient has no other medical problems or allergies. She takes no medications and does not use tobacco, alcohol, or drugs. The patient plays the violin for her high school orchestra and is the captain of her junior varsity tennis team. She is not sexually active. Her height is 175 cm (5 ft 8 in), weight is 65 kg (143 lb), and BMI is 21.2 kg/m<sup>2</sup>. Examination shows fully developed secondary sexual characteristics. Pelvic ultrasound shows a shortened vaginal canal with a rudimentary uterus. Which of the following is the most likely diagnosis in this patient?

- ☐ A. 21-hydroxylase deficiency
- ☐ B. Androgen insensitivity syndrome
- ☐ C. Kallmann syndrome
- ☐ D. Klinefelter syndrome
- ☐ E. Müllerian aplasia
- ☐ F. Triple X syndrome





had menarche at age 14. The patient has no other medical problems or allergies. She takes no medications and does not use tobacco, alcohol, or drugs. The patient plays the violin for her high school orchestra and is the captain of her junior varsity tennis team. She is not sexually active. Her height is 175 cm (5 ft 8 in), weight is 65 kg (143 lb), and BMI is 21.2 kg/m<sup>2</sup>. Examination shows fully developed secondary sexual characteristics. Pelvic ultrasound shows a shortened vaginal canal with a rudimentary uterus. Which of the following is the most likely diagnosis in this patient?

- ☐ A. ~~21-hydroxylase deficiency (3%)~~
- ☐ B. Androgen insensitivity syndrome (24%)
- ☐ C. Kallmann syndrome (6%)
- ☐ D. ~~Klinefelter syndrome (3%)~~
- ☒ E. Müllerian aplasia (58%)
- ☐ F. ~~Triple X syndrome (3%)~~

Correct

58%



02 mins, 12 secs



01/11/2021

Block Time Remaining: 00:14:56

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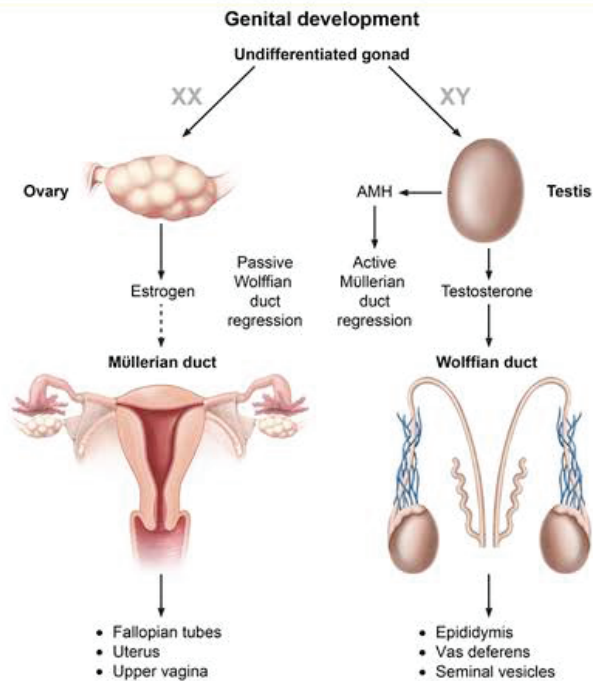
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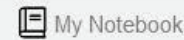
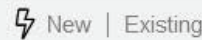
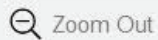
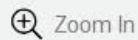
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### Exhibit Display



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• Upper vagina

• Seminal vesicles

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The sexually undifferentiated embryo at <6 weeks gestation has 2 pairs of genital ducts: the paramesonephric (Müllerian) ducts and the mesonephric (Wolffian) ducts. In the normal female (XX) fetus, the Müllerian ducts give rise to the fallopian tubes, uterus, cervix, and upper vagina by 20 weeks gestation. The Wolffian ducts degenerate from the lack of hormonal stimulation.

This patient is most likely a 46,XX female with Müllerian aplasia, also known as vaginal agenesis or Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome. Aplasia is defined as defective development or congenital absence of an organ or tissue, and patients with MRKH have **variable uterine development** and **no upper vagina** (eg, short vagina). As the uterus is hypoplastic or absent, the patient cannot menstruate (eg, **primary amenorrhea**). Patients with MRKH have **normal ovaries**, which secrete estrogen normally and enable **regular development of secondary sexual characteristics** (eg, breast, pubic hair).

Other Müllerian defects may result from inappropriate fusion of the Müllerian ducts (eg, unicornuate, bicornuate, and septate uterus). All females with Müllerian defects should undergo renal ultrasound, as up to 50% will have a coexisting urologic anomaly (eg, unilateral **renal agenesis**).

**(Choice A)** Congenital adrenal hyperplasia is most commonly due to 21-hydroxylase deficiency and has a variable presentation depending on the severity of the enzyme deficiency. Neonates typically have



to 50% will have a coexisting urologic anomaly (eg, unilateral renal agenesis).

**(Choice A)** Congenital adrenal hyperplasia is most commonly due to 21-hydroxylase deficiency and has a variable presentation depending on the severity of the enzyme deficiency. Neonates typically have virilization and life-threatening hyponatremia (salt-wasting). Late-onset 21-hydroxylase deficiency usually presents as hirsutism, oligomenorrhea, and acne.

**(Choice B)** Patients with **androgen insensitivity syndrome (AIS)** are 46,XY males who appear phenotypically female due to an androgen receptor defect. In contrast to patients with MRKH, patients with AIS have minimal axillary or pubic hair due to androgen resistance. In addition, patients with AIS have cryptorchid testes and no uterus or ovaries.

**(Choice C)** **Kallmann syndrome** occurs due to decreased synthesis of gonadotropin-releasing hormone (GnRH) in the hypothalamus (hypogonadotropic hypogonadism). Although females are rarely affected, those with the condition present with primary amenorrhea, no secondary sexual characteristics, and an olfactory sensory defect.

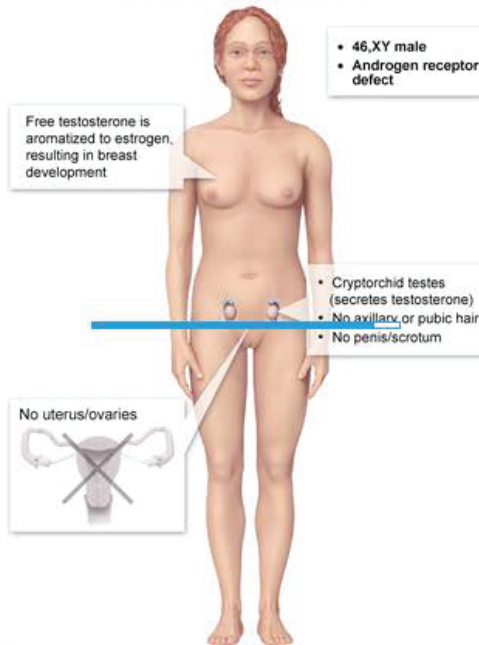
**(Choice D)** **Klinefelter syndrome** (47,XXY) affects males and is characterized by tall stature, poorly developed secondary sexual characteristics, atrophic testes, and infertility.

**(Choice F)** Patients with a 47,XXX karyotype may have a tall stature and slightly decreased IQ scores.

to 50% will have a coexisting urologic anomaly (eg, unilateral renal agenesis).

### Exhibit Display

#### Androgen insensitivity syndrome



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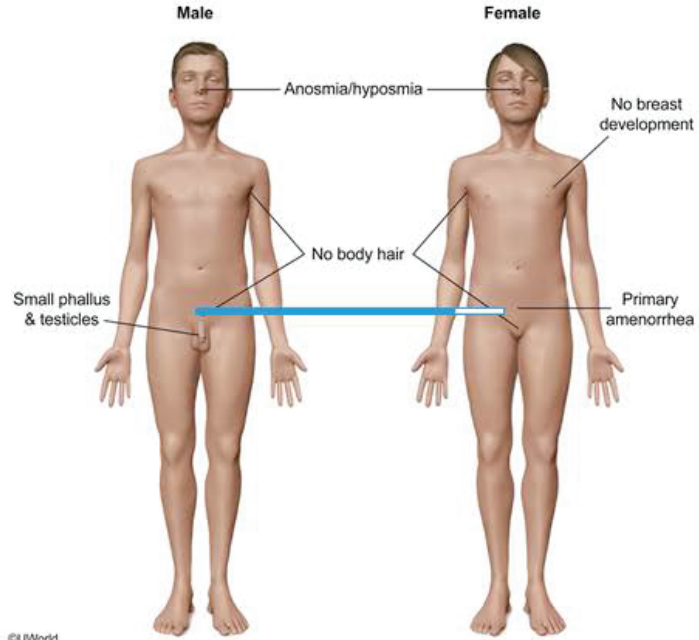




to 50% will have a coexisting urologic anomaly (eg, unilateral renal agenesis).

Exhibit Display

Kallmann syndrome





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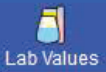
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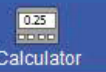
Tutorial



Lab Values



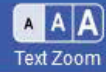
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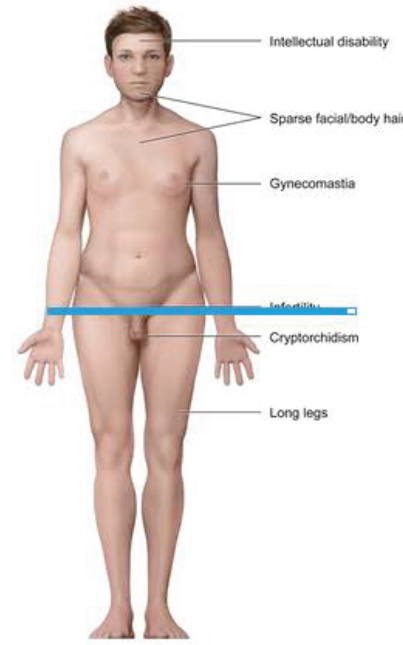


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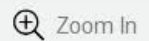
to 50% will have a coexisting urologic anomaly (eg, unilateral renal agenesis).

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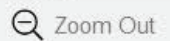
#### Klinefelter syndrome (47,XXY)



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Feedback



Suspend



End Block



cryptorchid testes and no uterus or ovaries.

**(Choice C)** Kallmann syndrome occurs due to decreased synthesis of gonadotropin-releasing hormone (GnRH) in the hypothalamus (hypogonadotropic hypogonadism). Although females are rarely affected, those with the condition present with primary amenorrhea, no secondary sexual characteristics, and an olfactory sensory defect.

**(Choice D)** Klinefelter syndrome (47,XXY) affects males and is characterized by tall stature, poorly developed secondary sexual characteristics, atrophic testes, and infertility.

**(Choice F)** Patients with a 47,XXX karyotype may have a tall stature and slightly decreased IQ scores. Physical features are typically normal, including sexual development.

### Educational objective:

Patients with Müllerian aplasia (ie, Mayer-Rokitansky-Küster-Hauser syndrome) have no upper vagina (eg, short vagina) and variable uterine development. These patients are 46,XX females with normal ovaries and secondary sexual characteristics.

### References

- ACOG Committee opinion: no. 562: müllerian agenesis: diagnosis, management, and treatment.







A 46-year-old woman comes to the office due to sexual difficulties for the past year. The patient rarely thinks about sex anymore and frequently declines sex when her husband tries to initiate. She is attracted to her husband and worries that he assumes she is losing interest in him. Although vaginal lubrication is adequate during sex and the patient can reach orgasm, she finds that her mind wanders during the experience. She is unsure what is causing a decrease in her sex drive, although she notes that she received a promotion 3 months ago and has been working longer hours since then. The patient describes her marriage as stable and loving. She has a history of a depressive episode and currently takes bupropion. Physical examination and laboratory studies, including thyroid function tests, show no abnormalities. Which of the following is the most likely diagnosis?

- ☐ A. Adjustment disorder
- ☐ B. Antidepressant-induced sexual dysfunction
- ☐ C. Female orgasmic disorder
- ☐ D. Female sexual interest/arousal disorder
- ☐ E. Genito-pelvic pain/penetration disorder

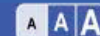




thinks about sex anymore and frequently declines sex when her husband tries to initiate. She is attracted to her husband and worries that he assumes she is losing interest in him. Although vaginal lubrication is adequate during sex and the patient can reach orgasm, she finds that her mind wanders during the experience. She is unsure what is causing a decrease in her sex drive, although she notes that she received a promotion 3 months ago and has been working longer hours since then. The patient describes her marriage as stable and loving. She has a history of a depressive episode and currently takes bupropion. Physical examination and laboratory studies, including thyroid function tests, show no abnormalities. Which of the following is the most likely diagnosis?

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- ☐ D. Female sexual interest/arousal disorder
- ☐ E. Genito-pelvic pain/penetration disorder
- ☐ F. Normal menopausal changes





adequate during sex and the patient can reach orgasm, she finds that her mind wanders during the experience. She is unsure what is causing a decrease in her sex drive, although she notes that she received a promotion 3 months ago and has been working longer hours since then. The patient describes her marriage as stable and loving. She has a **history** of a **depressive** episode and currently takes **bupropion**. Physical examination and laboratory studies, including thyroid function tests, show no abnormalities. Which of the following is the most likely diagnosis?

- ☐ A. Adjustment disorder (22%)
- ☐ B. Antidepressant-induced sexual dysfunction (13%)
- ☐ C. Female orgasmic disorder (0%)
- ☒ D. Female sexual interest/arousal disorder (48%)
- ☐ E. Genito-pelvic pain/penetration disorder (0%)
- ☐ F. Normal menopausal changes (14%)

Correct



48%

Answered correctly



01 min, 12 secs

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This patient's lack of sexual desire is most consistent with **female sexual interest/arousal disorder**, a sexual disorder characterized by lack of, or significantly reduced, sexual interest and/or arousal. Diagnosis requires ruling out psychological, medical, and substance/medication-related causes of sexual dysfunction (eg, depression, diabetes, chronic alcohol or drug use) and relationship problems.

The diagnosis of female sexual interest/arousal disorder encompasses symptoms of **decreased interest, decreased arousal, or both**. This patient primarily experiences decreased interest (ie, lack of sexual thoughts; reduced initiation of sexual activity or receptivity to a partner's attempts to initiate, but adequate lubrication/orgasm). Symptoms related to arousal may include decreased excitement/pleasure in response to mental and physical sexual cues and encounters.

**(Choice A)** Although the patient mentions that her condition is worse since her promotion 3 months ago, there is evidence of a change in sexual functioning preceding this stressful event.

**(Choice B)** Serotonergic antidepressants (eg, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors) are a common cause of medication-induced sexual dysfunction and can cause decreased libido as well as anorgasmia in women. This patient, however, is taking bupropion, a norepinephrine-dopamine reuptake inhibitor that does not affect serotonin and is unlikely to cause sexual side effects.





cause decreased libido as well as anorgasmia in women. This patient, however, is taking bupropion, a norepinephrine-dopamine reuptake inhibitor that does not affect serotonin and is unlikely to cause sexual side effects.

**(Choice C)** Female orgasmic disorder is characterized by marked delay in, decreased frequency and intensity of, or absence of orgasms.

**(Choice E)** Genitopelvic pain/penetration disorder involves recurrent difficulties with pain or fear of pain with vaginal intercourse or penetration attempts.

**(Choice F)** Although declining levels of estrogen in peri- and post-menopausal women may be associated with decreased sexual interest in some patients, this is typically accompanied by decreased vaginal lubrication, which this woman does not describe.

### Educational objective:

Female sexual interest/arousal disorder is characterized by lack of, or significantly reduced, sexual interest and/or arousal. Diagnosis requires ruling out psychological, medical, and substance/medication-related causes and relationship problems.

### References

- [Hypoactive sexual desire disorder: International Society for the Study of Women's Sexual Health](#)





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Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 24-year-old obese woman comes to the office due to spotting after vaginal intercourse. She also has some yellow vaginal discharge. The patient has taken oral contraceptive pills for the past 3 years and no other medications. Her paternal grandmother was diagnosed with cervical cancer at age 67. The patient's BMI is 35 kg/m<sup>2</sup>. On examination, the abdomen is soft and nontender. Speculum examination reveals purulent discharge from the cervical os. The cervix is friable. There is no cervical motion tenderness on bimanual examination and the adnexa are nontender. Microscopy of the discharge demonstrates abundant neutrophils, and nucleic acid amplification testing is positive. If left untreated, the patient's condition could lead to which of the following complications?

- ☐ A. Cervical cancer
- ☐ B. Cervical insufficiency
- ☐ C. Endometrial hyperplasia
- ☐ D. Infertility
- ☐ E. Ovarian cancer



1



Feedback



Suspend



End Block





some yellow vaginal discharge. The patient has taken oral contraceptive pills for the past 3 years and no other medications. Her paternal grandmother was diagnosed with cervical cancer at age 67. The patient's BMI is 35 kg/m<sup>2</sup>. On examination, the abdomen is soft and nontender. Speculum examination reveals purulent discharge from the cervical os. The cervix is friable. There is no cervical motion tenderness on bimanual examination and the adnexa are nontender. Microscopy of the discharge demonstrates abundant neutrophils, and nucleic acid amplification testing is positive. If left untreated, the patient's condition could lead to which of the following complications?

- ☐ A. Cervical cancer (17%)
- ☐ B. Cervical insufficiency (2%)
- ☐ C. Endometrial hyperplasia (2%)
- ☒ D. Infertility (76%)
- ☐ E. Ovarian cancer (0%)

Correct

76%



01 min, 29 secs



11/06/2020

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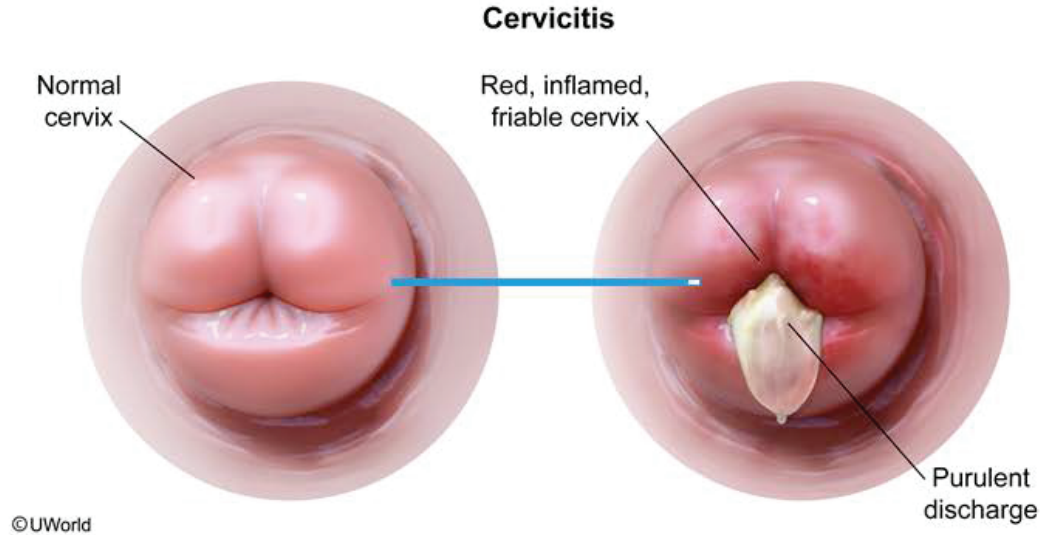
Gonococcal cervicitis	
Clinical features	<ul style="list-style-type: none"> <li>Purulent or mucopurulent discharge</li> <li>Friable cervix with easy bleeding (eg, intermenstrual or postcoital bleeding)</li> </ul>
Diagnosis	Nucleic acid amplification testing
Empiric treatment	3rd-generation cephalosporin PLUS Azithromycin or doxycycline

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This patient has an **endocervical infection (cervicitis)**, which is classically **asymptomatic** and detected by pelvic examination and **nucleic acid amplification testing**. When symptomatic, it presents with a mucopurulent discharge or intermenstrual or post-coital spotting. ***Neisseria gonorrhoeae*** and ***Chlamydia trachomatis*** are the most common pathogens, and untreated infection can ascend to the upper genital tract, resulting in **pelvic inflammatory disease (PID)**.

Treatment with **azithromycin and ceftriaxone** provides coverage of both organisms and prevents the

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tract, resulting in **pelvic inflammatory disease (PID)**.

Treatment with **azithromycin and ceftriaxone** provides coverage of both organisms and prevents the progression of infection to the uterus and fallopian tubes. Up to 20% of PID cases can result in tubal factor **infertility** due to permanent **scarring of the fallopian tubes** from salpingitis. PID also increases the risk for future ectopic pregnancies.

**(Choices A and B)** Gonococcal and chlamydial infections are not risk factors for cervical cancer. Family history is also not a risk factor for cervical cancer. However, infection with human papillomavirus strains 16 and 18 predisposes to cervical dysplasia and malignant transformation. High-grade cervical lesions require excision before they progress to cancer, but these procedures can cause cervical insufficiency and preterm labor.

**(Choice C)** Endometrial hyperplasia presents as dysfunctional uterine bleeding. Elevated estrogen without opposition by progesterone stimulates growth of the uterine lining. Obesity is a risk factor for endometrial hyperplasia due to excess aromatization of androgens to estrogen in the adipose tissue.

**(Choice E)** Use of combination oral contraceptive pills decreases ovarian cancer risk. Cervicitis is not a risk factor for ovarian cancer.



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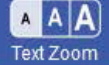
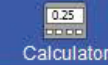
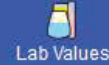
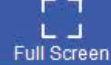
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labor.

**(Choice C)** Endometrial hyperplasia presents as dysfunctional uterine bleeding. Elevated estrogen without opposition by progesterone stimulates growth of the uterine lining. Obesity is a risk factor for endometrial hyperplasia due to excess aromatization of androgens to estrogen in the adipose tissue.

**(Choice E)** Use of combination oral contraceptive pills decreases ovarian cancer risk. Cervicitis is not a risk factor for ovarian cancer.

### Educational objective:

*Neisseria gonorrhoeae* and *Chlamydia trachomatis* cause mucopurulent cervicitis, which can progress to pelvic inflammatory disease (PID) if untreated. PID can cause scarring of the fallopian tubes, leading to ectopic pregnancy and infertility.

### References

- [Sexually transmitted diseases treatment guidelines, 2015.](#)

Microbiology

Female Reproductive System &amp; Breast

Cervicitis

Subject

System

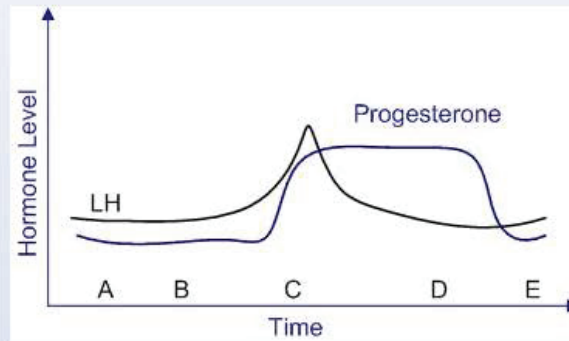
Topic

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A 26-year-old woman, para 0, comes to the office for follow-up of irregular menstrual periods. She has a period every 15-90 days that lasts 2-14 days and ranges from spotting to quarter-sized clots. The patient and her husband have been trying to conceive, but it has been difficult to time intercourse given her erratic menstrual cycles. She has been exercising and losing weight and now has a BMI of 32 kg/m<sup>2</sup>.

Gynecologic examination shows normal external genitalia, a small mobile uterus, and normal adnexa. Endometrial sampling reveals coiled glands filled with carbohydrate-rich mucus, edematous stroma, and tortuous spiral arteries. At which time point on the graph below was the endometrial sampling most likely obtained?

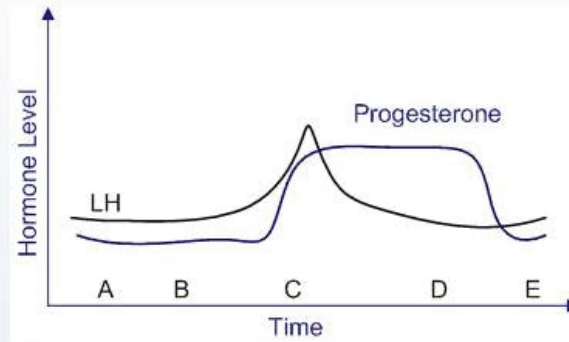


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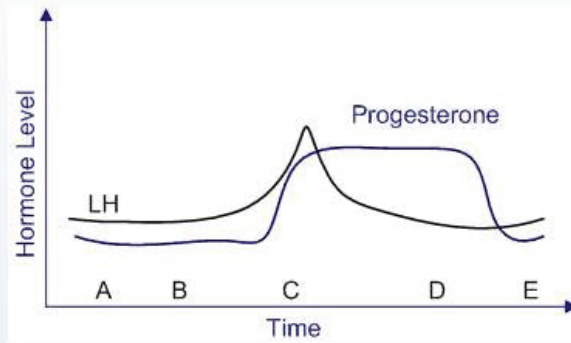


obtained?

☐ A.A☐ B.B☒ C.C☐ D.D☐ E.E**Submit**



obtained?



- ☐ A.A (0%)
- ☐ B.B (2%)
- ☐ C.C (12%)
- ☒ D.D (82%)
- ☐ E.E (1%)



Mark



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Tutorial



Lab Values



Notes



Calculator



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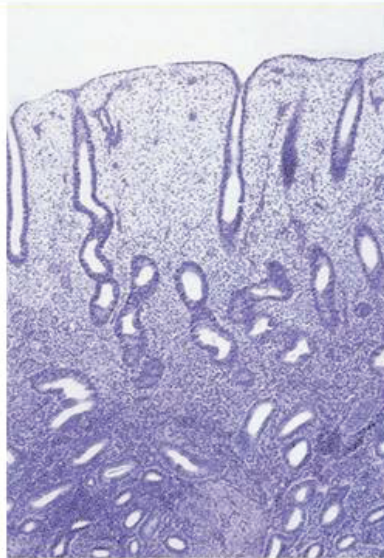


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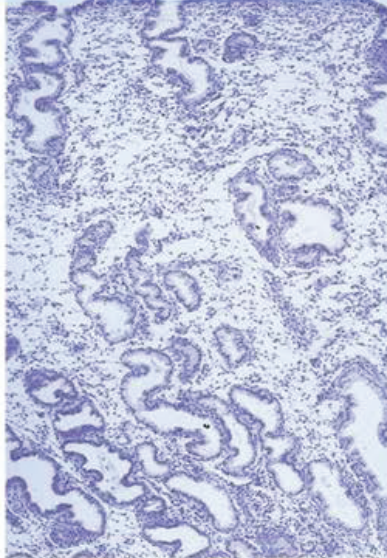


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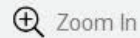


**Mid-proliferative phase endometrium (day 7).**  
The endometrium demonstrates uniform development, with a gland:stroma ratio of less than 1:1. The glands are straight and narrow, and contain small lumens.

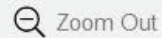


**Mid-secretory phase endometrium (day 21).**  
The gland:stroma ratio has increased to approximately 1:1 because the amplified stromal volume is associated with marked stromal edema. The glands are dilated and coiled, and contain wide lumens.

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edemat. The glands are dilated and crowded, and contain wide lumens.

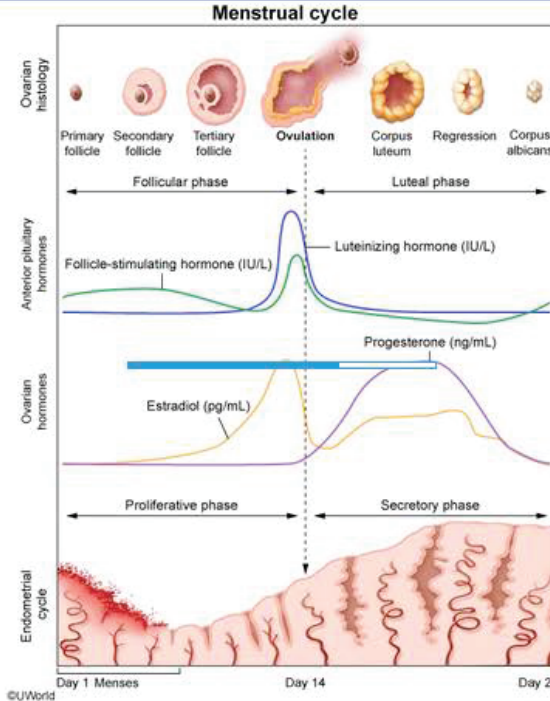
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The uterine **endometrium** is a highly specialized mucosa that undergoes histologic transformation during the menstrual cycle in preparation for zygote implantation. The upper layer of the endometrium (the stratum functionale) consists of lamina propria studded with tubular glands, spiral arteries, and dilated capillaries. Histologic examination of these components with an endometrial biopsy allows for endometrial dating and evaluation for pathological processes.

A normal **menstrual cycle** lasts for 21-35 days (28+/-7 days). The **proliferative phase** is the first half of the menstrual cycle (**days 1-14**), beginning with the first day of menses and ending with ovulation. During this time, estrogen stimulates proliferation of the stratum functionale. Normal proliferative endometrium consists of nonbranching, nonbudding, uniform glands evenly distributed throughout a uniform stroma (**Choices A and E**). In the midproliferative phase (**Choice B**), the glands are tubular, narrow, and lined with pseudostratified, elongated, mitotically active epithelial cells. The stratum functionale contains compact, nonedematous stroma. The uterine glands have increased in length and girth but still remain relatively straight. No secretions are present in the glandular lumens. The endometrium thickens, but the coiled spiral arteries remain limited to the deeper layers. At the end of the proliferative phase, ovulation occurs. Endometrial biopsy at ovulation shows a late proliferative endometrium with coiled glands and



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coiled spiral arteries remain limited to the deeper layers. At the end of the proliferative phase, ovulation occurs. Endometrial biopsy at ovulation shows a late proliferative endometrium with coiled glands and occasional cytoplasmic vacuoles in the glandular epithelium (**Choice C**).

The **secretory phase** is the second half of the menstrual cycle (**days 15-28**), which follows ovulation. During this time, progesterone secreted by the corpus luteum in the ovary promotes the development of secretory endometrium. The glands increase in size and become more coiled, and the cells lining the glands acquire large cytoplasmic vacuoles. Glycogen-rich mucus is released into the glandular lumens. The stroma becomes increasingly edematous, and the prominent spiral arteries extend to the endometrial surface. The endometrial biopsy taken in this patient is consistent with the mid-secretory phase.

### Educational objective:

The secretory phase of the menstrual cycle occurs between ovulation and menses, from days 15-28 of the normal menstrual cycle. Progesterone released by the corpus luteum causes the uterine glands to coil and secrete glycogen-rich mucus in preparation for embryo implantation. The endometrial stroma becomes edematous and completely traversed by tortuous spiral arteries that extend from the deeper layers to the uterine lumen.

### References







A 24-year-old woman comes to the office due to 2 days of burning during urination and increased urinary frequency and urgency. The patient has had no fever, chills, nausea, vomiting, flank pain, or vaginal discharge, but reports darkening of the urine. She has no other medical conditions and does not use tobacco, alcohol, or drugs. The patient is sexually active with her boyfriend and takes an oral contraceptive for birth control. Vital signs are within normal limits. Physical examination shows mild suprapubic tenderness. There is no costovertebral angle tenderness. Which of the following pathogens is most likely responsible for this patient's symptoms?

- ☐ A. *Candida albicans*
- ☐ B. *Chlamydia trachomatis*
- ☐ C. *Escherichia coli*
- ☐ D. *Gardnerella vaginalis*
- ☐ E. Group B streptococcus
- ☐ F. *Klebsiella pneumoniae*
- ☐ G. *Neisseria gonorrhoeae*





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responsible for this patient's symptoms?

- ☐ A. *Candida albicans*
- ☐ B. *Chlamydia trachomatis*
- ☐ C. *Escherichia coli*
- ☐ D. *Gardnerella vaginalis*
- ☐ E. Group B streptococcus
- ☐ F. *Klebsiella pneumoniae*
- ☐ G. *Neisseria gonorrhoeae*
- ☐ H. *Proteus mirabilis*
- ☐ I. *Pseudomonas aeruginosa*
- ☐ J. *Staphylococcus aureus*

Submit

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tenderness. There is no costovertebral angle tenderness. Which of the following pathogens is most likely

responsible for this patient's symptoms?

- ☐ A. *Candida albicans* (1%)
- ☐ B. *Chlamydia trachomatis* (3%)
- ☒ C. *Escherichia coli* (86%)
- ☐ D. *Gardnerella vaginalis* (0%)
- ☐ E. Group B streptococcus (1%)
- ☐ F. *Klebsiella pneumoniae* (0%)
- ☐ G. *Neisseria gonorrhoeae* (1%)
- ☐ H. *Proteus mirabilis* (3%)
- ☐ I. *Pseudomonas aeruginosa* (0%)
- ☐ J. *Staphylococcus aureus* (0%)







## Explanation

This patient with painful urination, urinary frequency/urgency, and suprapubic tenderness has **acute cystitis**, a urinary tract infection (UTI) confined to the bladder. Most cases arise when **fecal organisms** gain access to the urethral meatus and subsequently ascend into the bladder. ***Escherichia coli***, a gram-negative coliform bacteria, causes >70% of UTIs; other Enterobacteriaceae organisms, such as *Klebsiella pneumoniae* and *Proteus mirabilis* (**Choices F and H**), are also common but much less so than *E coli*. **Women** develop UTIs much more often than men due to the proximity of the anus and vaginal introitus and the short length of the female urethra.

**(Choice A)** *Candida albicans* is a common cause of vulvovaginitis, which usually presents with vaginal discharge, burning, and pruritis.

**(Choices B and G)** *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are leading sexually transmitted pathogens. Although urethritis symptoms (eg, dysuria) can occur, most symptomatic women have significant mucopurulent vaginal discharge. Suprapubic tenderness is less common.

**(Choice D)** Bacterial vaginosis occurs when normal vaginal flora (eg, *Lactobacillus*) is replaced with facultative anaerobes such as *Gardnerella vaginalis*. Most cases are asymptomatic, but some individuals have thin, whitish vaginal discharge and a fishy vaginal odor.





pathogens. Although urethritis symptoms (eg, dysuria) can occur, most symptomatic women have significant mucopurulent vaginal discharge. Suprapubic tenderness is less common.

**(Choice D)** Bacterial vaginosis occurs when normal vaginal flora (eg, *Lactobacillus*) is replaced with facultative anaerobes such as *Gardnerella vaginalis*. Most cases are asymptomatic, but some individuals have thin, whitish vaginal discharge and a fishy vaginal odor.

**(Choice E)** Group B streptococcus commonly colonizes the genital and gastrointestinal tract and rarely causes infection. However, it can be passed to infants during vaginal birth, leading to early neonatal sepsis.

**(Choices I and J)** *Pseudomonas aeruginosa* and *Staphylococcus aureus* are uncommon UTI pathogens in healthy, young women. However, they can cause cystitis in those who have recently received antibiotics or have been hospitalized. Both organisms are much less common than *E coli*.

### Educational objective:

Urinary tract infections are most common in women and are typically caused by enteric pathogens.

*Escherichia coli* is the leading pathogen.

Microbiology

Female Reproductive System &amp; Breast

Urinary tract infection





Mark



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Settings

A 22-year-old woman comes to the emergency department with dysuria, vulvar pain, and itching. She has felt feverish and fatigued for the last few days. She has a new sexual partner and has been using a hormonal vaginal ring to prevent pregnancy. The patient had chlamydia 3 years ago and was treated with antibiotics. Physical examination reveals inguinal lymphadenopathy and tender vesicular lesions covering both labia majora and the perineum. This patient's infection can lead to which of the following conditions?

- ☐ A. Facial nerve palsy
- ☐ B. Locomotor ataxia
- ☐ C. Postherpetic neuralgia
- ☐ D. Recurrent genital ulcers
- ☐ E. Squamous cell vulvar carcinoma

**Submit**

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Feedback

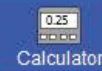
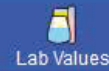


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A 22-year-old woman comes to the emergency department with **dysuria**, vulvar pain, and itching. She has felt feverish and fatigued for the last few days. She has a new sexual partner and has been using a hormonal vaginal ring to prevent pregnancy. The patient had chlamydia 3 years ago and was treated with antibiotics. Physical examination reveals inguinal lymphadenopathy and tender vesicular lesions covering both labia majora and the perineum. This patient's infection can lead to which of the following conditions?

- ☐ A. Facial nerve palsy (1%)
- ☐ B. Locomotor ataxia (2%)
- ☐ C. Postherpetic neuralgia (16%)
- ☒ D. Recurrent genital ulcers (68%)
- ☐ E. Squamous cell vulvar carcinoma (10%)

Correct

 68%  
Answered correctly

 01 min, 12 secs  
Time Spent

 01/30/2021  
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## Genital herpes

<b>Etiology</b>	HSV-2 (most common)
<b>Clinical presentation</b>	<ul style="list-style-type: none"><li>• Cluster of painful vesicles, pustules &amp;/or ulcers on labia, penis, buttocks, or thigh</li><li>• <math>\pm</math> Systemic symptoms in primary infection</li></ul>
<b>Treatment</b>	Acyclovir, famciclovir, or valacyclovir

**HSV** = herpes simplex virus.

Herpes is one of the most common **sexually transmitted** diseases. This patient's systemic symptoms (eg, **fever**, myalgia); **inguinal lymphadenopathy**; and itchy, painful, vesicular genital rash are typical of **primary genital herpes**. Genital herpes is most commonly caused by **herpes virus type 2 (HSV-2)**. The characteristic rash on the genitalia or **buttocks** occurs in stages - **vesicles**, **ulcers**, and then **crusting**.

Following infection, HSV lies dormant in the sacral dorsal root ganglia and can be reactivated to cause **recurrent genital lesions**. Recurrence tends to be localized and less severe due to humoral immunity from prior infection. Patients are more contagious during a recurrence, and barrier contraception prevents





Mark



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Lab Values



Notes



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Settings

Herpes is one of the most common **sexually transmitted** diseases. This patient's systemic symptoms (eg, **fever**, myalgia); **inguinal lymphadenopathy**; and itchy, painful, vesicular genital rash are typical of **primary genital herpes**. Genital herpes is most commonly caused by **herpes virus type 2 (HSV-2)**. The characteristic rash on the genitalia or **buttocks** occurs in stages - **vesicles**, **ulcers**, and then **crusting**.

Following infection, HSV lies dormant in the sacral dorsal root ganglia and can be reactivated to cause **recurrent genital lesions**. Recurrence tends to be localized and less severe due to humoral immunity from prior infection. Patients are more contagious during a recurrence, and barrier contraception prevents spread.

**(Choice A)** Facial nerve palsy can be a neurological manifestation of Lyme disease (caused by the spirochete *Borrelia burgdorferi*) or HSV-1. HSV-1 typically causes oral rather than genital vesicles. Lyme disease typically causes fatigue, anorexia, headache, and occasional fever, without a vesicular rash.

**(Choice B)** Untreated syphilis can infect the dorsal roots of the spinal column and lead to tertiary neurosyphilis characterized by tabes dorsalis (locomotor ataxia) and general paresis. Primary syphilis typically presents with a single painless genital lesion (**chancre**) after initial infection with *Treponema pallidum* spirochete.

**(Choice C)** Varicella zoster virus also invades the dorsal root sensory ganglia, and reactivation from the



1



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End Block



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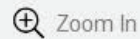


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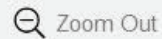


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## Exhibit Display



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1



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typically presents with a single painless genital lesion (chancere) after initial infection with *Treponema pallidum* spirochete.

**(Choice C)** Varicella zoster virus also invades the dorsal root sensory ganglia, and reactivation from the dorsal root ganglia causes herpes zoster (eg, shingles). A complication of shingles is postherpetic neuralgia (persistent pain after resolution of lesions). Typical presentation of herpes zoster is a painful vesicular rash in a dermatomal distribution without systemic involvement, in contrast to this patient with bilateral vesicular lesions and fever.

**(Choice E)** Human papillomavirus is an oncogenic double-stranded DNA virus that exclusively infects the epithelial cells, predisposing to the development of cervical and vulvar carcinoma. Warts are the most common skin manifestation.

### Educational objective:

Primary infection with herpes simplex virus type 2 (HSV-2) typically presents with fever and a painful vesicular genital rash. HSV-2 primarily infects the sacral dorsal root ganglia and can be reactivated to cause recurrent genital lesions.

### References

- Current concepts for genital herpes simplex virus infection: diagnostics and pathogenesis of genital tract



1



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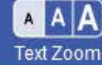
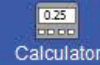
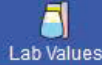
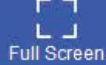


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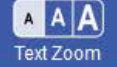
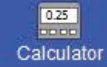
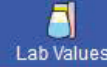


A 16-year-old, previously healthy girl comes to the office due to vaginal discharge that began 5 days ago. The discharge is grayish-white and fishy smelling. The patient is sexually active with a male partner and occasionally uses condoms. Temperature is 36.7 C (98.1 F), blood pressure is 106/52 mm Hg, and pulse is 78/min. Examination shows a small amount of grayish discharge in the vaginal vault. The cervix appears normal. Which of the following would most likely be seen on wet mount microscopy?

- ☐ A. Epithelial cells covered with bacteria
- ☐ B. Epithelial cells with rare leukocytes
- ☐ C. Gram-negative intracellular diplococci
- ☐ D. Leukocytes and pear-shaped organisms
- ☐ E. Pseudohyphae with leukocytes

Submit






A 16-year-old, previously healthy girl comes to the office due to vaginal discharge that began 5 days ago. The discharge is grayish-white and fishy smelling. The patient is sexually active with a male partner and occasionally uses condoms. Temperature is 36.7 C (98.1 F), blood pressure is 106/52 mm Hg, and pulse is 78/min. Examination shows a small amount of grayish discharge in the vaginal vault. The cervix appears normal. Which of the following would most likely be seen on wet mount microscopy?

- ☒ A. Epithelial cells covered with bacteria (75%)
- ☐ B. Epithelial cells with rare leukocytes (4%)
- ☐ C. Gram-negative intracellular diplococci (4%)
- ☐ D. Leukocytes and pear-shaped organisms (11%)
- ☐ E. Pseudohyphae with leukocytes (3%)

Correct

 75%  
Answered correctly

 01 min, 41 secs  
Time Spent







 09/04/2020  
Last Updated



# Differential diagnosis of vaginitis

## Exhibit Display

### Differential diagnosis of vaginitis

Bacterial vaginosis ( <i>Gardnerella vaginalis</i> )	Trichomoniasis ( <i>Trichomonas vaginalis</i> )	Candida vaginitis ( <i>Candida albicans</i> )
		
<ul style="list-style-type: none"><li>Thin, off-white discharge with fishy odor</li><li>No inflammation</li></ul>	<ul style="list-style-type: none"><li>Thin, yellow-green, malodorous, frothy discharge</li><li>Vaginal inflammation</li></ul>	<ul style="list-style-type: none"><li>Thick, "cottage cheese" discharge</li><li>Vaginal inflammation</li></ul>
		
<ul style="list-style-type: none"><li>pH &gt;4.5</li><li>Clue cells</li><li>Positive whiff test (amine odor with KOH)</li></ul>	<ul style="list-style-type: none"><li>pH &gt;4.5</li><li>Motile trichomonads</li></ul>	<ul style="list-style-type: none"><li>Normal pH (3.8 - 4.5)</li><li>Pseudohyphae</li></ul>
Metronidazole or clindamycin	Metronidazole; treat sexual partner	Fluconazole

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pH >4.5

pH >4.5

Normal pH (3.8 - 4.5)



or clindamycin

partner

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This patient's clinical presentation is most consistent with **bacterial vaginosis** (BV). BV is caused by an **imbalance of the vaginal bacterial flora** (eg, decreased lactobacilli colonization) and is associated with sexual activity, cigarette smoking, and vaginal douching. The decreased lactobacilli colonization causes a subsequent **increase in vaginal pH** and overgrowth of anaerobic bacteria (eg, *Gardnerella vaginalis*), which generate malodorous amines. The amines cause the characteristic **grayish-white, fishy-smelling discharge** with no associated vaginal inflammation.

Wet mount microscopy of the discharge shows **clue cells** (squamous epithelial cells with **adherent bacteria**). Application of potassium hydroxide to the discharge produces an amine odor (ie, positive whiff test). Treatment is with **metronidazole** or **clindamycin**.

**(Choice B)** A wet mount with epithelial cells and rare leukocytes is consistent with normal vaginal discharge (ie, physiologic leukorrhea). Physiologic leukorrhea is not malodorous.

**(Choice C)** Gram stain showing gram-negative intracellular diplococci is consistent with *Neisseria gonorrhoeae* cervicitis, which is characterized by cervical erythema, friability, and purulent cervical discharge.



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Lab Values



Notes



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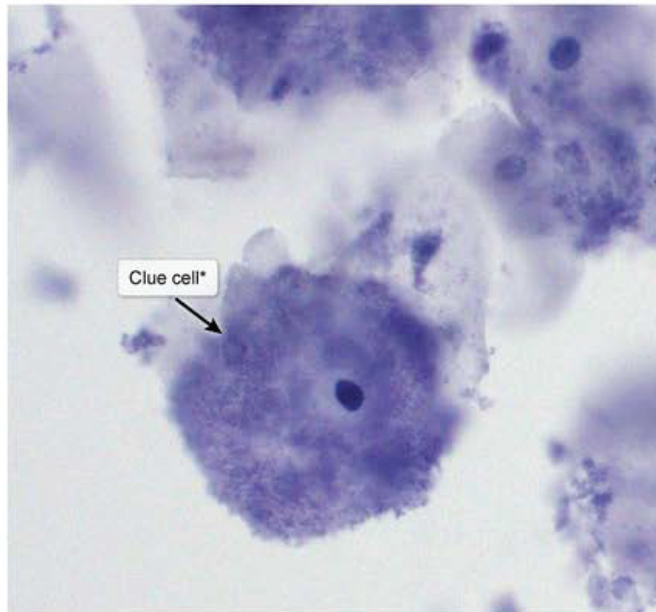
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or clindamycin

partner

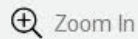
## Exhibit Display

## Bacterial vaginosis

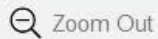


\*Squamous cell with adherent bacteria (eg. Gardnerella)

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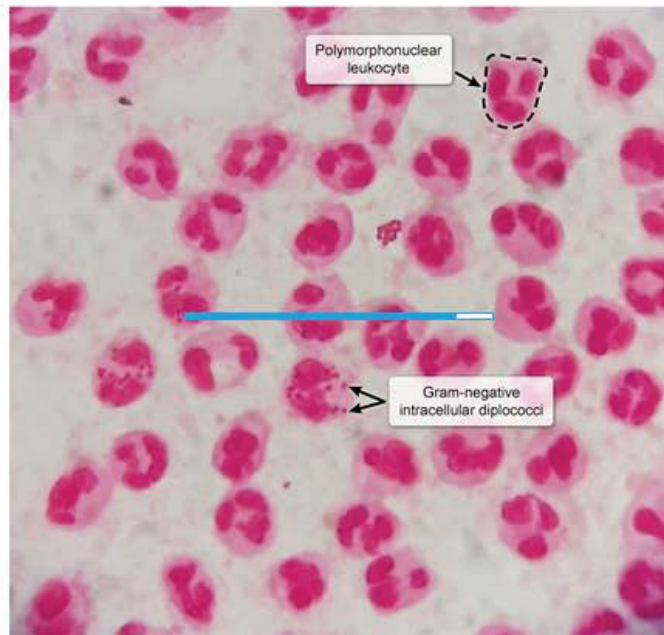
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or clindamycin

partner

### Exhibit Display

#### *Neisseria gonorrhoeae*



Polymorphonuclear leukocyte

Gram-negative intracellular diplococci

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*gonorrhoeae* cervicitis, which is characterized by cervical erythema, friability, and purulent cervical discharge.

**(Choice D)** A wet mount of *trichomoniasis* would show leukocytes and pear-shaped organisms (flagellated trophozoites). *Trichomonas* vaginitis typically presents with vulvovaginal erythema and frothy, yellow-green vaginal discharge; patients with *Trichomonas* cervicitis classically have a cervix with punctate hemorrhage (ie, strawberry cervix).

**(Choice E)** Pseudohyphae with leukocytes are seen in *Candida* vaginitis, which would present with thick, white vaginal discharge and associated vaginal inflammation (eg, vaginal erythema, pruritus).

### Educational objective:

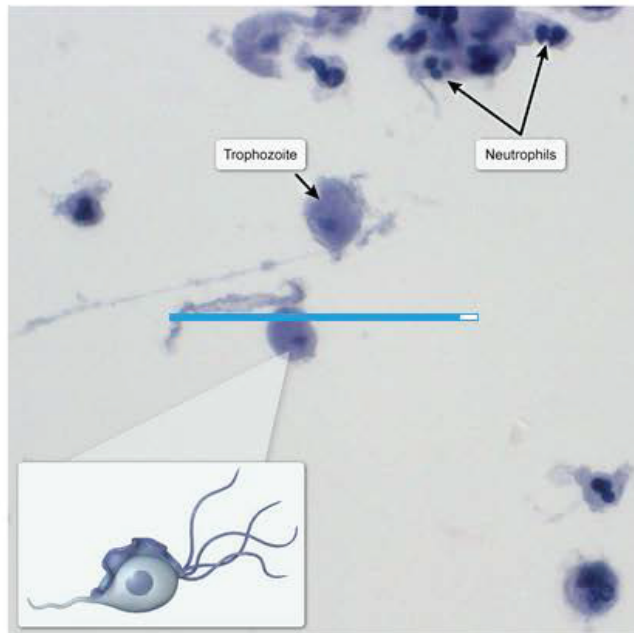
Bacterial vaginosis is caused by a disruption of the vaginal bacterial flora and is characterized by a thin, gray-white, malodorous vaginal discharge. Clue cells (squamous epithelial cells with adherent bacteria) are seen on wet mount microscopy.

### References

- [Vaginitis.](#)

### Exhibit Display

*Trichomonas vaginalis*



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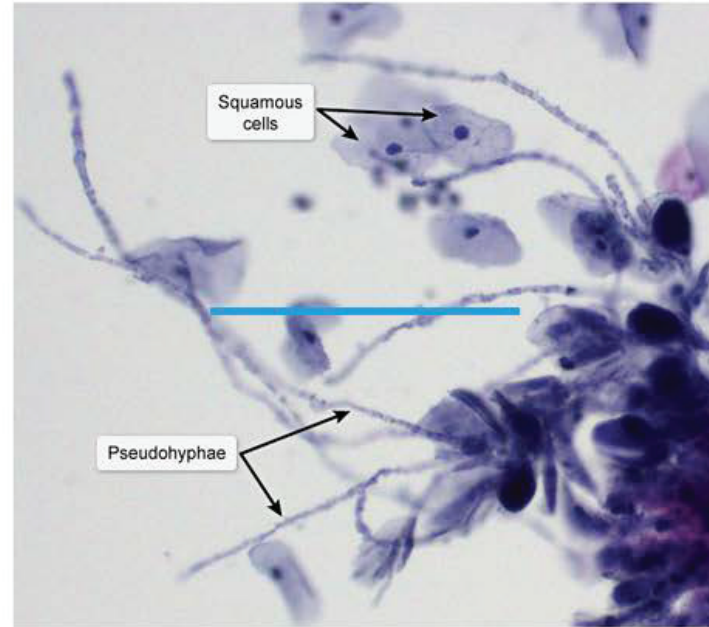
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*Candida*



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Settings

A 10-year-old girl is brought to the office for evaluation of short stature. She was an average-sized infant, but over the past few years, her height growth velocity has plateaued. The patient has not menstruated and has no symptoms. She takes no medications, has no allergies, and has received all recommended immunizations. Menarche occurred in her mother at age 14 and both of her parents are tall. The patient's height is at the <5th percentile and weight is at the 50th percentile for age and sex. She has no breast buds and no axillary or pubic hair. She has a low hairline, a short and wide neck, a broad chest, and widely spaced nipples. Which of the following is the most likely underlying mechanism for this patient's condition?

- ☐ A. Balanced translocation
- ☐ B. Frameshift mutation
- ☐ C. Meiotic nondisjunction
- ☐ D. Trinucleotide repeat expansion
- ☐ E. Uniparental disomy

**Submit**

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Settings

A 10-year-old girl is brought to the office for evaluation of **short stature**. She was an average-sized infant, but over the past few years, her height growth velocity has plateaued. The patient has not menstruated and has no symptoms. She takes no medications, has no allergies, and has received all recommended immunizations. Menarche occurred in her mother at age 14 and both of her parents are tall. The patient's height is at the <5th percentile and weight is at the 50th percentile for age and sex. She has no breast buds and no axillary or pubic hair. She has a low hairline, a short and wide neck, a **broad chest**, and widely spaced nipples. Which of the following is the most likely underlying mechanism for this patient's condition?

- ☐ A. Balanced translocation (1%)
- ☐ B. ~~Frameshift mutation~~ (1%)
- ☒ C. Meiotic nondisjunction (81%)
- ☐ D. ~~Trinucleotide repeat expansion~~ (0%)
- ☒ E. Uniparental disomy (15%)

Incorrect

Correct answer



81%

Answered correctly



01 min, 31 secs

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09/08/2020

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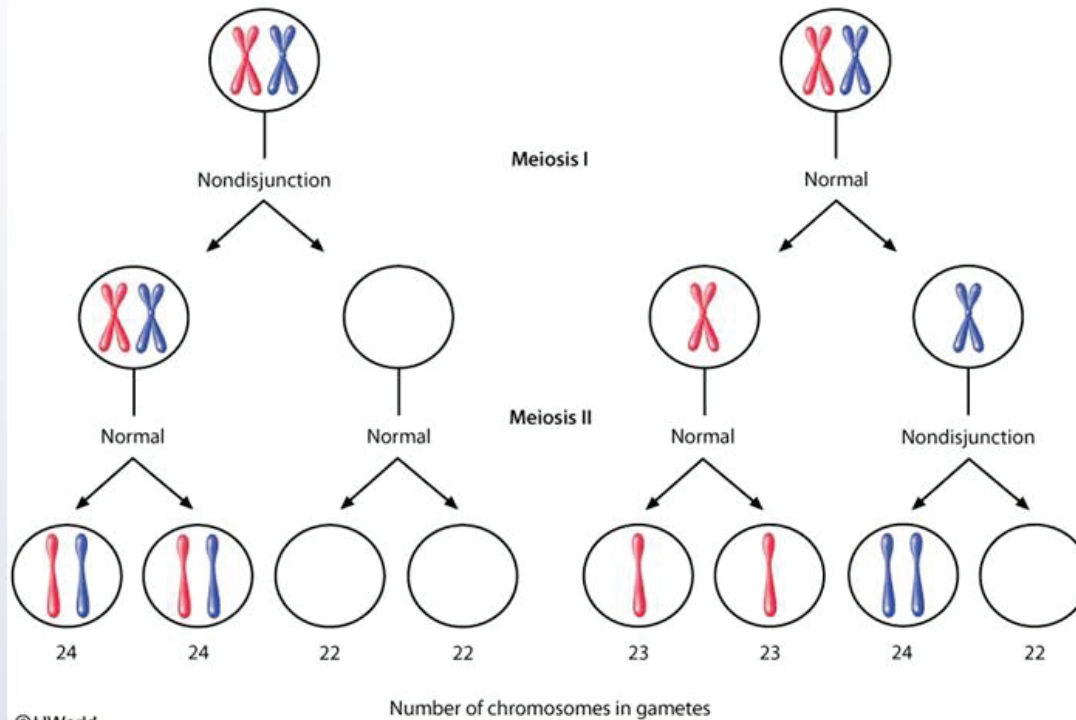


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### Nondisjunction in meiosis



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Turner syndrome is a genetically heterogeneous condition that is most commonly due to **meiotic nondisjunction** during gametogenesis. The loss of one X chromosome in the sperm or egg results in a missing X chromosome in all of the patient's cells (**45,X**). In other patients, the nondisjunction event occurs during mitosis in early embryogenesis; these patients are missing the X chromosome in only some of their cells (mosaic Turner syndrome [45,X/46,XX]). A minority of patients have both X chromosomes, but one is structurally abnormal and missing some genetic material (eg, X fragments, isochromosomes).

The loss of all or part of the X chromosome in Turner syndrome results in a **missing SHOX gene**, which normally promotes long bone growth. Therefore, patients with this syndrome typically have **short stature**. Meiotic nondisjunction is also responsible for Klinefelter syndrome and trisomies 13, 18, and 21.

**(Choice A)** A balanced translocation is clinically silent as there is no excess or shortage of genetic material. However, a parent with a balanced translocation is at risk for having a child with an unbalanced translocation. An unbalanced trisomy 21 (in which one chromosome 14 contains the long arms of both chromosomes 14 and 21) is responsible for 3%-4% of Down syndrome cases.

**(Choice B)** A frameshift mutation is a genetic mutation in which a number of nucleotides not divisible by 3 are inserted into or removed from a coding DNA sequence. As a result, the reading frame is shifted during protein translation, resulting in an entirely different peptide sequence (typically with formation of a





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**(Choice B)** A frameshift mutation is a genetic mutation in which a number of nucleotides not divisible by 3 are inserted into or removed from a coding DNA sequence. As a result, the reading frame is shifted during protein translation, resulting in an entirely different peptide sequence (typically with formation of a premature stop codon).

**(Choice D)** Trinucleotide repeat expansion is responsible for numerous diseases, including fragile X syndrome (CGG repeats), myotonic dystrophy (CTG repeats), and Huntington disease (CAG repeats).

**(Choice E)** **Uniparental disomy** occurs when an individual inherits 2 copies of a chromosome from one parent and no copies of the chromosome from the other parent. For instance, although most often due to chromosomal deletions, uniparental disomy can also cause Angelman and Prader-Willi syndromes due to loss of expression of maternal/paternal imprinted components of a critical region of chromosome 15.

### Educational objective:

Patients with Turner syndrome may have karyotype 45,X (complete monosomy), 45,X/46,XX (mosaicism), or 46,XX (with partial deletion of one X chromosome). Complete monosomy X usually results from meiotic nondisjunction during gametogenesis.

### References

- **Prader-Willi syndrome and Angelman syndrome.**



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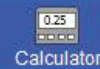
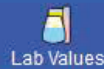
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A 23-year-old woman, gravida 2, para 1, comes to the labor and delivery unit at 39 weeks gestation with abdominal discomfort and regular contractions. The patient had an uncomplicated first pregnancy that resulted in a spontaneous vaginal delivery at full term 3 years ago, and the current pregnancy has been uncomplicated. She takes a prenatal vitamin daily and no other medications. In response to increasing estrogen levels, the myometrial cells start to express genes that encode connexin-43 and the oxytocin receptor. These molecular changes would result in increased formation of which of the following?

- ☐ A. Adherens junctions
- ☐ B. Desmosomes
- ☐ C. Fenestrae
- ☐ D. Gap junctions
- ☐ E. Hemidesmosomes
- ☐ F. Tight junctions

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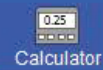
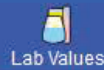
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- ☐ A. Adherens junctions (10%)
- ☐ B. Desmosomes (8%)
- ☐ C. Fenestrae (6%)
- ☒ D. Gap junctions (62%)
- ☐ E. Hemidesmosomes (3%)
- ☐ F. Tight junctions (9%)



Cell junctions		
Type	Proteins	Function
Gap junction	Connexins	Intercellular communication
Tight junction	Claudins, occludin	Paracellular barrier
Adherens junction	Cadherins	Cellular anchor
Desmosomes	Cadherins (eg, desmogleins, desmoplakin)	
Hemidesmosomes	Integrins	

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Initiation of labor requires a series of biochemical changes in the uterus and cervix mediated by endocrine changes. **Cell junctions** are multiprotein complexes that allow contact between adjacent cells or between a



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Initiation of labor requires a series of biochemical changes in the uterus and cervix mediated by endocrine changes. **Cell junctions** are multiprotein complexes that allow contact between adjacent cells or between a cell and the extracellular matrix. Communicating (gap) junctions are especially important during labor and delivery, which require coordination and synchronization of individual myometrial cells. Gap junctions permit diffusion of molecules between neighboring cellular cytoplasms through a connexon (cylinder with a central channel composed of 6 connexin proteins).

Immediately prior to delivery, **estrogen** stimulates upregulation of **gap junctions** between individual myometrial smooth muscle cells. An increase in gap junction density at delivery heightens **myometrial** excitability. Gap junctions consist of aggregated **connexin** proteins (eg, connexin-43) that allow passage of ions between myometrial cells.

Estrogen also increases expression of uterotonic (eg, oxytocin) receptors, which mediate calcium transport through ligand-activated calcium channels. The combination of an increase in gap junction density and uterotonic receptors results in coordinated, synchronous labor contractions.

**(Choices A and B)** Both adherens junctions and desmosomes are composed of cadherins and are involved in intercellular adhesion. The cytoplasmic anchor of adherens junctions is the actin filament, whereas the cytoplasmic anchor of desmosomes is the intermediate filament. Autoantibodies against



1



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**(Choices A and B)** Both adherens junctions and desmosomes are composed of cadherins and are involved in intercellular adhesion. The cytoplasmic anchor of adherens junctions is the actin filament, whereas the cytoplasmic anchor of desmosomes is the intermediate filament. Autoantibodies against desmoglein, a cadherin protein for desmosomes, are found in [pemphigus vulgaris](#).

**(Choice C)** Fenestrae are gaps between endothelial cells that allow for paracellular transport. Swollen fenestrae in renal glomerular capillary endothelial cells are implicated in preeclampsia (presents with new-onset hypertension and proteinuria or end-organ dysfunction at  $\geq 20$  weeks gestation).

**(Choice E)** Hemidesmosomes link cells to the basement membrane via integrins, the transmembrane anchor proteins. Autoantibodies to these proteins cause [bullous pemphigoid](#) and [pemphigoid gestationis](#).

**(Choice F)** Tight junctions are comprised of claudins and occludin and serve as paracellular barriers to water and solutes. The enterotoxin from *Clostridium perfringens*, a common cause of food poisoning, binds claudin and interferes with tight junctions in the intestinal barrier. Water loss from the tissue to the intestinal lumen results in watery diarrhea.

### Educational objective:

Gap junctions facilitate communication and coordination between cells and play an important role in labor contractions. Connexins are proteins that assemble into gap junctions and their density increases in the



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whereas the cytoplasmic anchor of desmosomes is the intermediate filament. Autoantibodies against desmoglein, a cadherin protein for desmosomes, are found in **pemphigus vulgaris**.

**(Choice C)** Fenestrae are gaps between endothelial cells that allow for paracellular transport. Swollen fenestrae in renal glomerular capillary endothelial cells are implicated in preeclampsia (presents with new-onset hypertension and proteinuria or end-organ dysfunction at  $\geq 20$  weeks gestation).

**(Choice E)** Hemidesmosomes link cells to the basement membrane via integrins, the transmembrane anchor proteins. Autoantibodies to these proteins cause **bullous pemphigoid** and **pemphigoid gestationis**.

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### Educational objective:

Gap junctions facilitate communication and coordination between cells and play an important role in labor contractions. Connexins are proteins that assemble into gap junctions and their density increases in the uterus before delivery in response to rising estrogen levels.

### References





Mark



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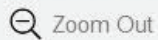


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## References

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## References

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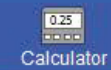
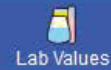
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A 24-year-old woman comes to the emergency department due to lower abdominal cramping and vaginal bleeding. The patient started to have vaginal spotting a few days ago but has had slightly increased bleeding with painful lower abdominal cramping since this morning. She is sexually active, and her last menstrual period was 5 weeks ago. Blood pressure is 130/80 mm Hg and pulse is 100/min. Diffuse tenderness to palpation is present over the lower abdomen. On speculum examination, the cervix is closed and there is dark red blood coming from the cervical os. Bimanual examination reveals a small uterus and a 3-cm mass in the left adnexa. Quantitative serum  $\beta$ -hCG level is 1,200 mIU/mL (normal: <5). Which of the following is the most likely underlying cause of this patient's presentation?

- ☐ A. Abnormal ovum fertilization by 2 sperm
- ☐ B. Benign proliferation of the uterine myometrium
- ☐ C. Endometrial tissue development within the ovary
- ☐ D. Implantation of a fertilized embryo in the fallopian tube
- ☐ E. Torsion of an ovarian mass containing ectoderm, endoderm, and mesoderm







bleeding. The patient started to have vaginal spotting a few days ago but has had slightly increased bleeding with painful lower abdominal cramping since this morning. She is sexually active, and her last menstrual period was 5 weeks ago. Blood pressure is 130/80 mm Hg and pulse is 100/min. Diffuse tenderness to palpation is present over the lower abdomen. On speculum examination, the cervix is closed and there is dark red blood coming from the cervical os. Bimanual examination reveals a small uterus and a 3-cm mass in the left adnexa. Quantitative serum  $\beta$ -hCG level is 1,200 mIU/mL (normal: <5). Which of the following is the most likely underlying cause of this patient's presentation?

- ☐ A. Abnormal ovum fertilization by 2 sperm (12%)
- ☐ B. Benign proliferation of the uterine myometrium (0%)
- ☐ C. Endometrial tissue development within the ovary (1%)
- ☒ D. Implantation of a fertilized embryo in the fallopian tube (82%)
- ☐ E. Torsion of an ovarian mass containing ectoderm, endoderm, and mesoderm (2%)

Correct

82%



01 min



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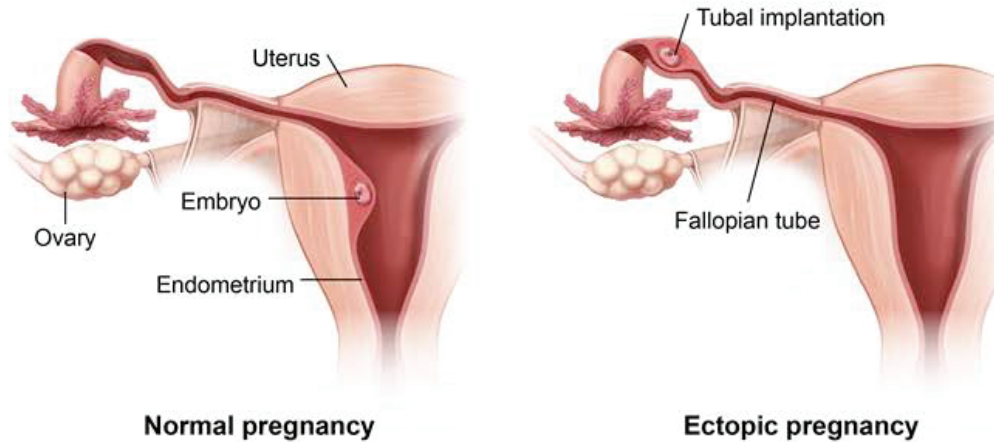


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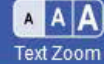
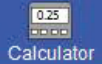
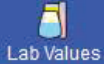
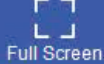
## Ectopic pregnancy



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This patient has lower abdominal pain and vaginal bleeding. In the setting of a **positive pregnancy test** (eg, detectable  $\beta$ -hCG) and an **adnexal mass**, her presentation is most concerning for **ectopic pregnancy**.

Following ovulation, the ovum normally travels along the length of the fallopian tube where it can be fertilized by a sperm cell. The fertilized ovum continues through the fallopian tube, developing into a



Pregnancy.

Following ovulation, the ovum normally travels along the length of the fallopian tube where it can be fertilized by a sperm cell. The fertilized ovum continues through the fallopian tube, developing into a blastocyst, and subsequently implants on the uterine endometrium. However, migration of the fertilized ovum is occasionally impeded, resulting in **implantation in the fallopian tube** (~90%) or other **extrauterine locations**. Ectopic pregnancy often occurs secondary to tubal pathology (eg, pelvic inflammatory disease, prior pelvic surgery) but can present in patients without risk factors.

After implantation in the fallopian tube, the ectopic pregnancy develops into a highly vascular adnexal mass that draws blood flow from surrounding tissues to maintain its rapid growth. This causes ischemic injury to surrounding tissues, fallopian tube edema, and potential tubal rupture, resulting in the classic symptoms of **pelvic cramping** and **vaginal bleeding** (eg, spotting).

**(Choice A)** A hydatidiform mole can occur due to abnormal ovum fertilization by 2 sperm and may present with vaginal bleeding and adnexal enlargement (ie, theca lutein cyst formation due to  $\beta$ -hCG stimulation). Patients typically have an enlarged uterus (due to abundant growth of chorionic villi) and markedly elevated  $\beta$ -hCG levels ( $>100,000$  mIU/mL), neither of which is seen in this patient.

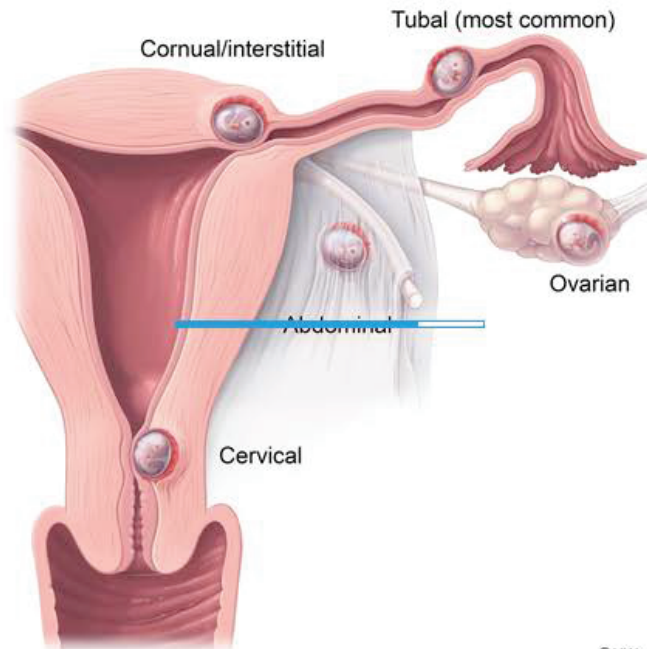
**(Choice B)** Uterine leiomyoma (ie, **fibroids**) are tumors arising from benign proliferation of the myometrium. Although they can cause cramping and vaginal bleeding, fibroids usually present with uterine





### Exhibit Display

## Ectopic pregnancy locations



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$\beta$ -hCG levels ( $>100,000$  mIU/mL), neither of which is seen in this patient.

**(Choice B)** Uterine leiomyoma (ie, **fibroids**) are tumors arising from benign proliferation of the myometrium. Although they can cause cramping and vaginal bleeding, fibroids usually present with uterine enlargement or an abnormal uterine contour, which are not seen in this patient. In addition, fibroids are not associated with elevated  $\beta$ -hCG levels.

**(Choice C)** An endometrioma, or ectopic endometrial tissue in the ovary, can cause an adnexal mass and vaginal bleeding if ruptured. However, patients typically have dysmenorrhea and additional symptoms associated with endometriosis (eg, dyspareunia, dyschezia).

**(Choice E)** Ovarian torsion can occur in patients with a mature teratoma (an ovarian mass composed of ectoderm, endoderm, and mesoderm). Although torsion can cause pelvic pain and a palpable adnexal mass, the pain is typically sudden and unilateral and vaginal bleeding is uncommon.

### Educational objective:

Ectopic pregnancy occurs when a fertilized embryo implants in an extrauterine location (eg, the fallopian tube). Patients can have pelvic cramping, vaginal bleeding, and a palpable adnexal mass.

### References

- [Incidence, diagnosis and management of tubal and nontubal ectopic pregnancies: a review.](#)





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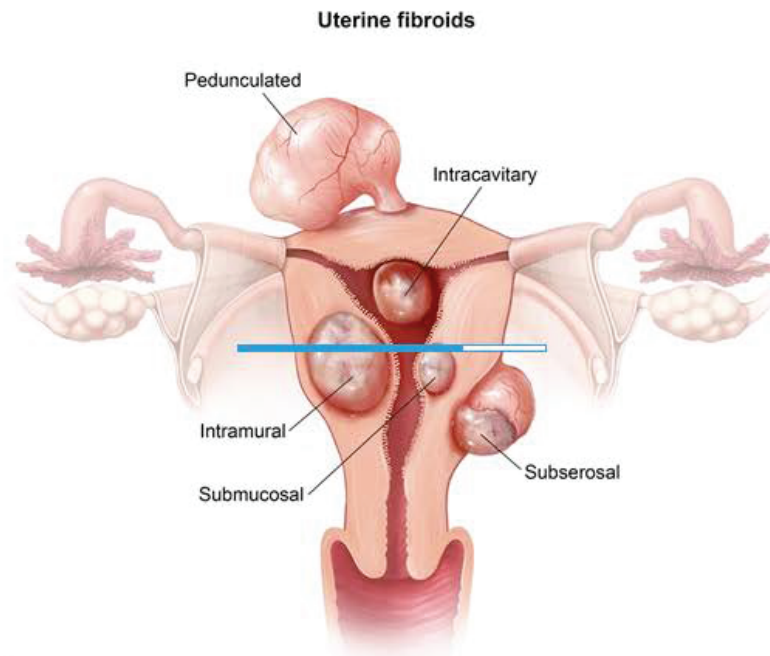
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β hCG levels (>100,000 mIU/mL), neither of which is seen in this patient.

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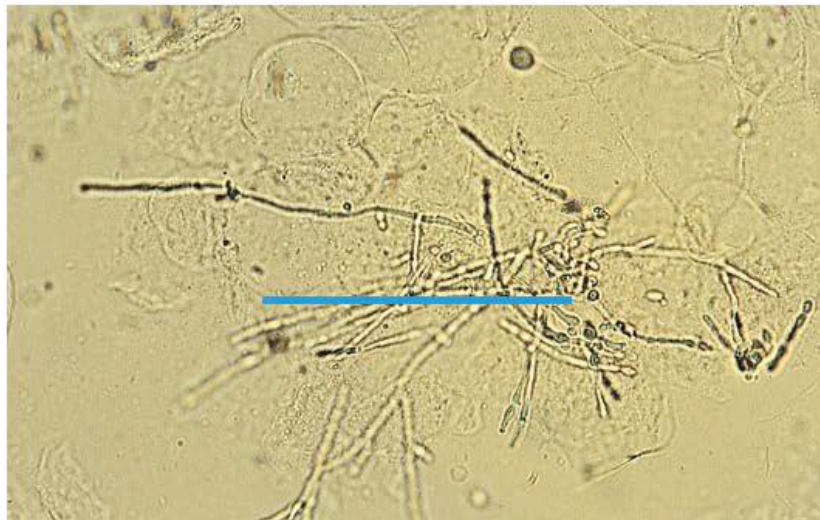


A 20-year-old woman comes to the office for increasing vaginal discharge and vulvar pruritus. The patient has had vaginal discharge for the past 4 days. She is sexually active with multiple partners and uses oral contraceptive pills. Vital signs are normal. Pelvic examination is performed, and wet mount microscopy of a vaginal swab is shown in the [exhibit](#). Which of the following is the most appropriate pharmacotherapy for this patient?

- ☐ A. Acyclovir
- ☐ B. Azithromycin
- ☐ C. Ceftriaxone
- ☐ D. Clindamycin
- ☐ E. Fluconazole
- ☐ F. Metronidazole

**Submit**

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A 20-year-old woman comes to the office for increasing vaginal discharge and vulvar pruritus. The patient has had vaginal discharge for the past 4 days. She is sexually active with multiple partners and uses oral contraceptive pills. Vital signs are normal. Pelvic examination is performed, and wet mount microscopy of a vaginal swab is shown in the [exhibit](#). Which of the following is the most appropriate pharmacotherapy for this patient?

- ☐ A. Acyclovir (0%)
- ☐ B. Azithromycin (0%)
- ☐ C. Ceftriaxone (0%)
- ☐ D. Clindamycin (0%)
- ☒ E. Fluconazole (87%)
- ☐ F. Metronidazole (10%)

Correct



87%

Answered correctly



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Time Spent



01/08/2021

Last Updated

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## Exhibit Display

### Differential diagnosis of vaginitis

Bacterial vaginosis ( <i>Gardnerella vaginalis</i> )	Trichomoniasis ( <i>Trichomonas vaginalis</i> )	Candida vaginitis ( <i>Candida albicans</i> )
		
<ul style="list-style-type: none"> <li>Thin, off-white discharge with fishy odor</li> <li>No inflammation</li> </ul>	<ul style="list-style-type: none"> <li>Thin, yellow-green, malodorous, frothy discharge</li> <li>Vaginal inflammation</li> </ul>	<ul style="list-style-type: none"> <li>Thick, "cottage cheese" discharge</li> <li>Vaginal inflammation</li> </ul>
		
<ul style="list-style-type: none"> <li>pH &gt;4.5</li> <li>Clue cells</li> <li>Positive whiff test (amine odor with KOH)</li> </ul>	<ul style="list-style-type: none"> <li>pH &gt;4.5</li> <li>Motile trichomonads</li> </ul>	<ul style="list-style-type: none"> <li>Normal pH (3.8 - 4.5)</li> <li>Pseudohyphae</li> </ul>
Metronidazole or clindamycin	Metronidazole; treat sexual partner	Fluconazole

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This patient's vulvar pruritus and vaginal discharge are consistent with **candidal vulvovaginitis**, an infection typically due to overgrowth of ***Candida albicans***. *C. albicans* is a yeast and a component of normal vaginal flora; however, alterations in the balance of normal vaginal flora can allow for excessive *Candida* proliferation and symptomatic infection. These imbalances can occur due to **increased estrogen** levels such as with estrogen-containing contraceptive use or pregnancy. Additional predisposing factors include recent **antibiotic use**, immunosuppression (eg, systemic corticosteroids), sexual activity, and **diabetes mellitus** (particularly if poorly controlled).

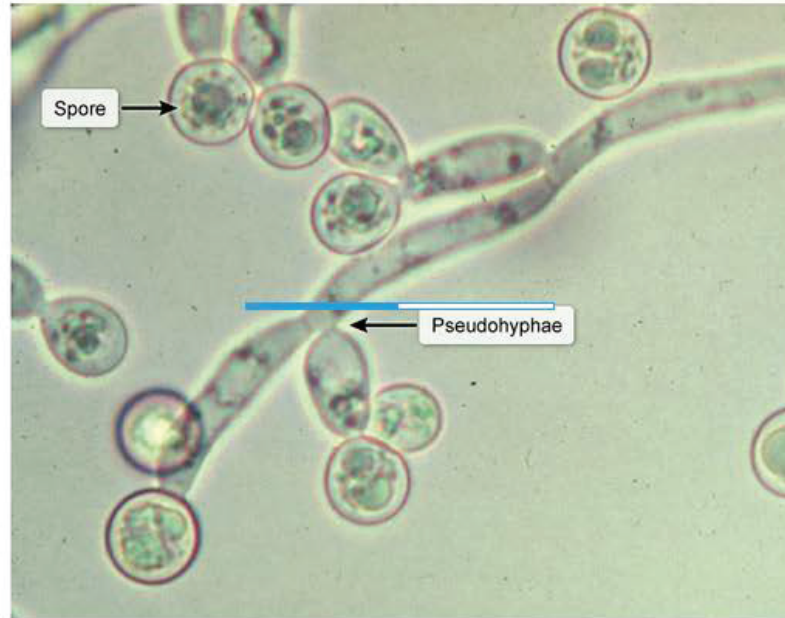
With *Candida* overgrowth, patients develop vulvovaginal inflammation that can result in erythema, pruritus, and a thick, white, clumpy vaginal discharge. Diagnosis is made via **wet mount microscopy**, which typically reveals **pseudohyphae with budding yeast** and true hyphae. Treatment of vulvovaginal candidiasis is with azole antifungal medications (eg, **fluconazole**), which decrease ergosterol synthesis and disrupt fungal cellular membrane formation.

**(Choice A)** Acyclovir is used to treat herpes simplex virus, which can occasionally cause multinucleated giant cells to be visualized on cervical cytology (rather than wet mount microscopy). Herpes simplex virus is a rare cause of cervicitis, and patients typically have concomitant, painful vulvovaginal vesicles.



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*Candida*



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giant cells to be visualized on cervical cytology (rather than wet mount microscopy). Herpes simplex virus is a rare cause of cervicitis, and patients typically have concomitant, painful vulvovaginal vesicles.

**(Choices B and C)** Azithromycin (a macrolide) and ceftriaxone (a third-generation cephalosporin) in combination are used to treat acute cervicitis due to *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. *C. trachomatis* cannot be easily visualized on microscopy due to its unusual peptidoglycan cell wall. *N. gonorrhoeae* is a gram-negative diplococcus that can be found intracellularly on microscopy.

**(Choices D and F)** Clindamycin and metronidazole are used to treat *Gardnerella vaginalis*, an anaerobic bacterium that causes bacterial vaginosis (BV). On wet mount microscopy, BV can be identified by **clue cells**, which are vaginal epithelial cells covered in bacteria. Metronidazole also treats *Trichomonas vaginalis*, a protozoan infection characterized by frothy, yellow-green vaginal discharge and motile, **flagellated trichomonads** on wet mount microscopy.

### Educational objective:

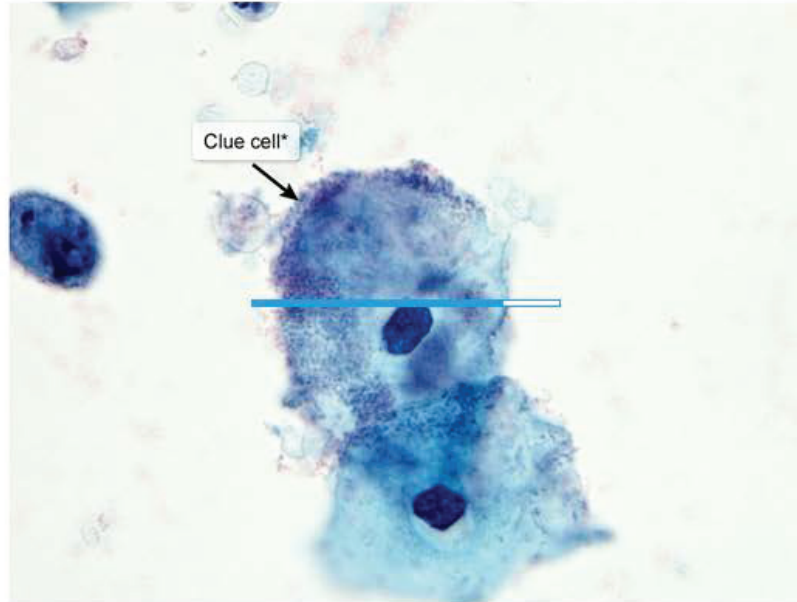
Vulvovaginal candidiasis typically presents with thick, white, clumpy vaginal discharge, vulvovaginal erythema and pruritus, and pseudohyphae on wet mount microscopy. Treatment is with an antifungal medication (eg, fluconazole).

### References



### Exhibit Display

#### Bacterial vaginosis



\*Epithelial cell covered with coccobacilli

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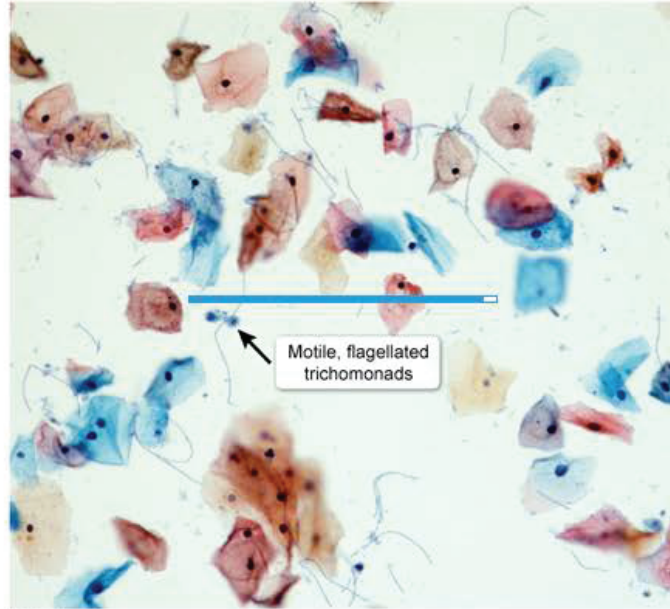
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#### References

### Exhibit Display

#### Trichomoniasis



Motile, flagellated trichomonads

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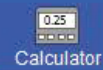
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#### References





A 65-year-old woman comes to the office due to intermittent leakage of urine. For the past 3 months, the patient has had to change her undergarments multiple times a day due to urine leakage. She voids 4 or 5 times during the day and occasionally wakes up at night to void. The patient has type 2 diabetes mellitus and was recently diagnosed with chronic obstructive pulmonary disease after evaluation for a chronic cough. Her only surgeries were 2 cesarean deliveries in her 20s. BMI is 30 kg/m<sup>2</sup>. Pelvic examination shows leakage of urine from the urethra during the Valsalva maneuver. Postvoid residual volume and urinalysis are normal. Which of the following is the most likely cause of this patient's clinical presentation?

- ☐ A. Decreased angle of the urethrovesical junction
- ☐ B. Fistula formation between the bladder and vagina
- ☒ C. Increased bladder sphincter sympathetic activity
- ☐ D. Reduced detrusor parasympathetic activity
- ☐ E. Weakened pelvic floor muscle support

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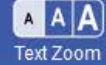
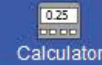
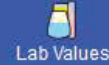
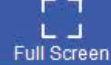
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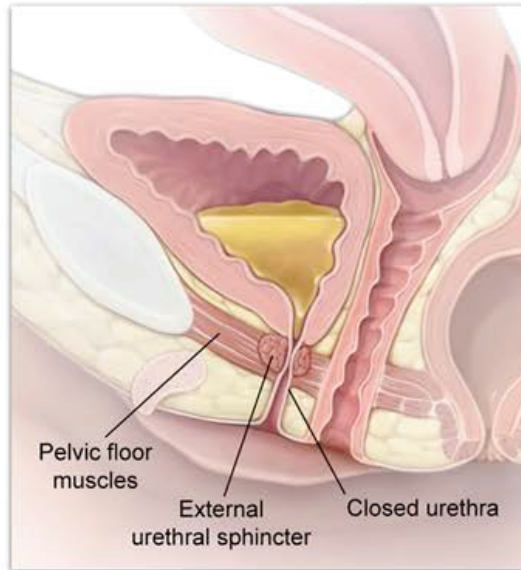
A 65-year-old woman comes to the office due to intermittent leakage of urine. For the past 3 months, the patient has had to change her undergarments multiple times a day due to urine leakage. She voids 4 or 5 times during the day and occasionally wakes up at night to void. The patient has type 2 diabetes mellitus and was recently diagnosed with chronic obstructive pulmonary disease after evaluation for a chronic cough. Her only surgeries were 2 cesarean deliveries in her 20s. BMI is 30 kg/m<sup>2</sup>. Pelvic examination shows leakage of urine from the urethra during the Valsalva maneuver. Postvoid residual volume and urinalysis are normal. Which of the following is the most likely cause of this patient's clinical presentation?

- ☐ A. Decreased angle of the urethrovesical junction (4%)
- ☐ B. Fistula formation between the bladder and vagina (1%)
- ☐ C. Increased bladder sphincter sympathetic activity (5%)
- ☐ D. Reduced detrusor parasympathetic activity (11%)
- ☒ E. Weakened pelvic floor muscle support (77%)

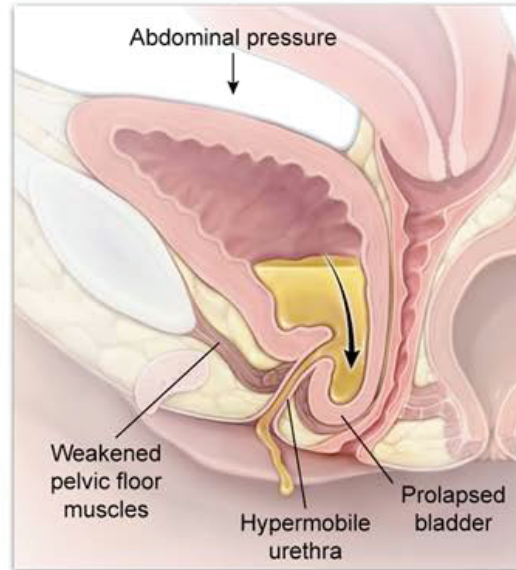


## Pelvic organ prolapse and urinary incontinence

Normal anatomy



Cystocele



This patient with intermittent leakage of urine likely has **stress urinary incontinence (SUI)**. In women, the





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urethra

This patient with intermittent leakage of urine likely has **stress urinary incontinence (SUI)**. In women, the **pelvic floor muscles** contract to stabilize the urethra against the anterior vaginal wall. This contraction decreases the angle between the bladder neck and the urethra (ie, urethrovesical angle), thereby compressing the urethra, stopping urine flow, and **maintaining continence**.

Chronically increased intrabdominal pressure (eg, obesity, **chronic cough** from COPD) can cause **weakened pelvic floor** muscle support. In addition, **prior pregnancies** (including cesarean deliveries) typically increase the laxity of pelvic floor muscles and connective tissue. In patients with SUI, the weakened pelvic floor muscles can no longer stabilize the urethra, leading to **urethral hypermobility**, an increased urethrovesical angle, and resultant urinary incontinence (**Choice A**). On examination, patients typically have leakage of urine during the Valsalva maneuver. Patients with severe pelvic floor laxity can also develop herniation of the bladder into the vagina (ie, cystocele), which further worsens SUI symptoms. Treatment can include pelvic floor muscle (ie, Kegel) exercises and pessary placement, which help support and maintain normal pelvic anatomy.

**(Choice B)** **Vesicovaginal fistula** is an abnormal connection between the bladder and vagina that most commonly occurs due to bladder injury from surgical or obstetric complications (eg, operative vaginal



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and maintain normal pelvic anatomy.

**(Choice B)** [Vesicovaginal fistula](#) is an abnormal connection between the bladder and vagina that most commonly occurs due to bladder injury from surgical or obstetric complications (eg, operative vaginal delivery). Unlike SUI, vesicovaginal fistulas cause continuous urinary dribbling rather than intermittent urinary leakage, and pelvic examination shows leakage of urine from the vagina (not the urethra).

**(Choices C and D)** The bladder receives both sympathetic and parasympathetic innervation to control continence and micturition. Sympathetic stimulation promotes urine storage and continence by increasing urethral sphincter tone. In contrast, parasympathetic activity stimulates detrusor muscle contraction and micturition. Therefore, increased bladder sphincter sympathetic activity or reduced detrusor parasympathetic activity would promote continence rather than the urinary leakage seen in this patient.

### Educational objective:

Stress urinary incontinence (intermittent, involuntary leakage of urine) is caused by weakened pelvic floor muscle support that often occurs due to chronically increased intraabdominal pressure (eg, obesity, chronic cough, prior pregnancies).

### References

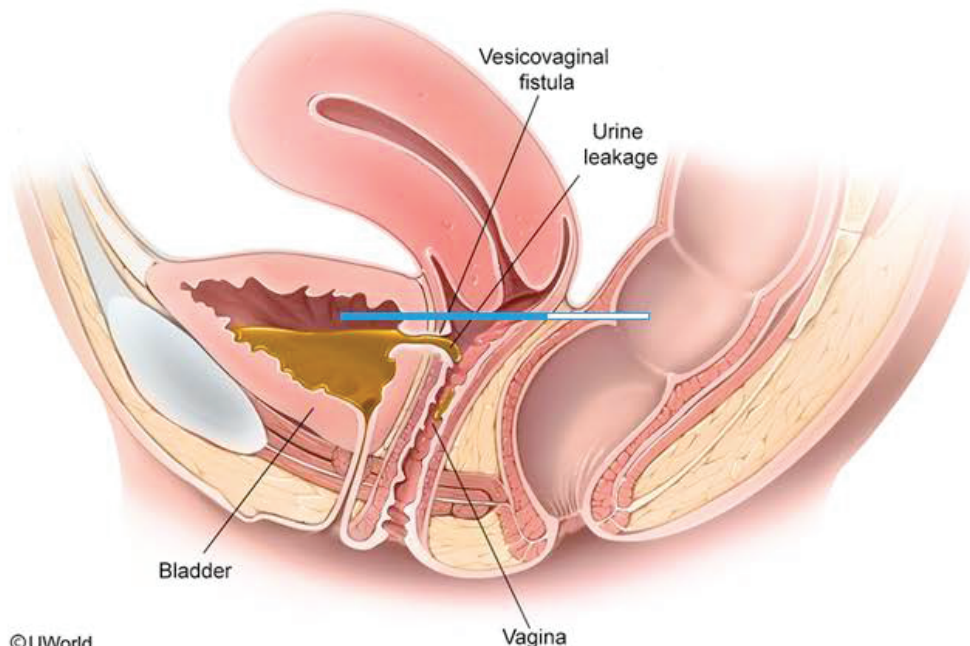
- [Diagnosis of urinary incontinence.](#)



and maintain normal pelvic anatomy

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Vesicovaginal fistula



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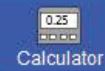
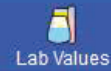




A 23-year-old female is being evaluated for infertility. Hormone studies reveal a normal rise in the blood estradiol level during the first phase of the menstrual cycle. Androgens synthesized in this patient's ovaries are converted to estradiol in which of the following cell types?

- ☐ A. Theca interna
- ☐ B. Theca externa
- ☐ C. Granulosa
- ☐ D. Oocyte
- ☐ E. Leydig

**Submit**




A 23-year-old female is being evaluated for infertility. Hormone studies reveal a normal rise in the blood estradiol level during the first phase of the menstrual cycle. Androgens synthesized in this patient's ovaries are converted to estradiol in which of the following cell types?

- ☐ A. Theca interna (13%)
- ☐ B. Theca externa (8%)
- ☒ C. Granulosa (72%)
- ☐ D. Oocyte (1%)
- ☐ E. Leydig (3%)

Correct

 72%  
Answered correctly

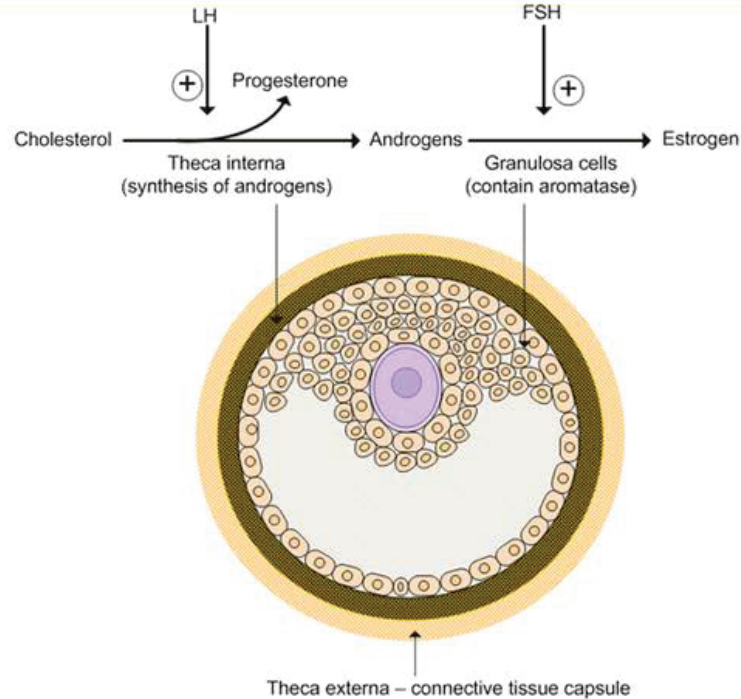
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Explanation



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## Theca externa – connective tissue capsule

Estradiol, the predominant estrogen in the human body, is primarily derived from androgens. Androgens and progesterone are synthesized from cholesterol in the theca interna cells under the influence of luteinizing hormone (LH). Androgens released from the theca interna cells migrate into the nearby granulosa cells, which contain the enzyme aromatase. Aromatase converts the androgens into estradiol. This reaction is stimulated by follicle stimulating hormone (FSH).

**(Choice B)** The theca externa lies outside of the theca interna and does not participate in steroidogenesis. The theca externa is composed of a layer of smooth muscle and fibroblast cells. It serves as a connective tissue support structure for the follicle.

**(Choice D)** Oocytes do not make the aromatase enzyme needed for conversion of androgens to estradiol. All female oocytes are formed during embryogenesis and remain arrested in prophase I until ovulation occurs. At each ovulation, a single oocyte completes meiosis I. Meiosis II occurs after fertilization.

**(Choice E)** Leydig cells are found only in the male testes. They are analogous in location and function to the theca interna cells of the ovarian follicle. Leydig cells are stimulated by LH to secrete testosterone.

**Educational Objective:**

LH stimulates the theca interna cells of the ovarian follicle to produce androgens. Aromatase within the





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**(Choice B)** The theca externa lies outside of the theca interna and does not participate in steroidogenesis. The theca externa is composed of a layer of smooth muscle and fibroblast cells. It serves as a connective tissue support structure for the follicle.

**(Choice D)** Oocytes do not make the aromatase enzyme needed for conversion of androgens to estradiol. All female oocytes are formed during embryogenesis and remain arrested in prophase I until ovulation occurs. At each ovulation, a single oocyte completes meiosis I. Meiosis II occurs after fertilization.

**(Choice E)** Leydig cells are found only in the male testes. They are analogous in location and function to the theca interna cells of the ovarian follicle. Leydig cells are stimulated by LH to secrete testosterone.

### Educational Objective:

LH stimulates the theca interna cells of the ovarian follicle to produce androgens. Aromatase within the follicle's granulosa cells subsequently converts these androgens to estradiol under FSH stimulation. The theca externa cells serve as a connective tissue support structure for the follicle.

Physiology

Female Reproductive System &amp; Breast

Infertility

Subject

System

Topic

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A 35-year-old nulliparous, mildly obese woman is diagnosed with cervical intraepithelial neoplasia III. She has been sexually active for 15 years and has had 4 lifetime partners. She has been monogamous with her current partner for several months and takes oral contraceptives consistently. The patient does not use condoms and douches regularly to "stay fresh." Menarche occurred at age 9, and her menses recur every 28 days and last 6 days. She had a plantar wart a few years ago but otherwise has no medical problems. She drinks 1-2 glasses of wine every night but does not use tobacco or illicit drugs. The patient's mother had breast cancer at age 42. Which of the following is the most significant factor that predisposed this patient to cervical abnormalities?

- ☐ A. Alcohol use
- ☒ B. Early menarche
- ☐ C. Family history of breast cancer
- ☐ D. History of plantar wart
- ☐ E. Lack of barrier contraception
- ☐ F. Nulliparity



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condoms and douches regularly to stay fresh. Menarche occurred at age 9, and her menses recur every 28 days and last 6 days. She had a plantar wart a few years ago but otherwise has no medical problems. She drinks 1-2 glasses of wine every night but does not use tobacco or illicit drugs. The patient's mother had breast cancer at age 42. Which of the following is the most significant factor that predisposed this patient to cervical abnormalities?

- ☐ A. Alcohol use
- ☐ B. Early menarche
- ☐ C. Family history of breast cancer
- ☐ D. History of plantar wart
- ☐ E. Lack of barrier contraception
- ☐ F. Nulliparity
- ☐ G. Obesity
- ☐ H. Practice of douching



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She drinks 1-2 glasses of **wine** every night but does not use tobacco or illicit drugs. The patient's mother had breast cancer at age 42. Which of the following is the most significant factor that predisposed this patient to cervical abnormalities?

- ☐ A. Alcohol use (0%)
- ☐ B. ~~Early menarche~~ (7%)
- ☐ C. ~~Family history of breast cancer~~ (5%)
- ☐ D. History of plantar wart (8%)
- ☒ E. Lack of barrier contraception (70%)
- ☐ F. ~~Nulliparity~~ (3%)
- ☒ G. Obesity (0%)
- ☐ H. ~~Practice of douching~~ (3%)

**Incorrect**

Correct answer



70%



01 min, 20 secs

Time spent



01/11/2021

Last updated

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HPV strains	Presentation
1-4	Skin warts (verruca vulgaris)
6, 11	Genital warts (condylomata acuminata)
16, 18	Cervical, vaginal, vulvar & anal neoplasia

HPV= human papillomavirus.

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**Squamous cell carcinoma (SCC)**, the most common type of cervical cancer, arises from the squamocolumnar junction of the endocervix. **Cervical intraepithelial neoplasia (CIN)** is **carcinoma in situ** and precedes SCC. CIN represents a wide spectrum of dysplastic changes of the cervical epithelium that occur under the influence of **human papillomavirus (HPV) infection**. CIN is usually transient in young healthy women. However, patients with persistent HPV infection or untreated high-grade CIN are at risk for invasive cervical cancer.

HPV strains 6 and 11 typically cause condylomata acuminata (genital warts) and have low malignancy potential. However, DNA from **high-risk strains (ie, 16, 18, and 31)** is integrated into the human cell







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HPV strains 6 and 11 typically cause condylomata acuminata (genital warts) and have low malignancy potential. However, DNA from **high-risk strains (ie, 16, 18, and 31)** is integrated into the human cell genome, leading to overexpression of **viral oncogenes E6 and E7**. E6 binds protein p53 and increases its degradation, whereas E7 binds to the retinoblastoma (*RB1*) gene and displaces transcription factors normally bound by pRB, the tumor suppressor protein product of *RB*.

Risk factors for developing cervical cancer are related to the risk of acquiring HPV infection. Although HPV can be transmitted by skin-to-skin contact, oncogenic strains are spread primarily by sexual contact. Therefore, this patient's most significant risk factors are a history of multiple sexual partners and the **lack of barrier contraceptive** (eg, condom) use.

**(Choice A)** Alcohol consumption increases the risk of liver and breast cancers, not cervical cancer.

**(Choices B, F, and G)** Nulliparity, early menarche, and obesity increase the risk of endometrial cancer. These factors are associated with increased estrogen stimulation of the endometrium.

**(Choice C)** Family history of breast cancer is a risk factor for developing breast malignancy. Breast cancer is not associated with cervical cancer, as the latter is usually due to a persistent, oncogenic HPV infection.

**(Choice D)** A plantar wart is usually caused by HPV strains 1-4; however, these strains are not typically



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**(Choice A)** Alcohol consumption increases the risk of liver and breast cancers, not cervical cancer.

**(Choices B, F, and G)** Nulliparity, early menarche, and obesity increase the risk of endometrial cancer.

These factors are associated with increased estrogen stimulation of the endometrium.

**(Choice C)** Family history of breast cancer is a risk factor for developing breast malignancy. Breast cancer is not associated with cervical cancer, as the latter is usually due to a persistent, oncogenic HPV infection.

**(Choice D)** A plantar wart is usually caused by HPV strains 1-4; however, these strains are not typically carcinogenic and are not associated with cervical dysplasia and invasive cervical cancer.

**(Choice H)** Douching is not a risk factor for HPV infection or cervical dysplasia/cancer. However, it is a risk factor for bacterial vaginosis. Douching disturbs the vaginal ecosystem, resulting in overgrowth of *Gardnerella vaginalis*.

### Educational objective:

Consistent use of barrier contraceptives is extremely important for preventing sexually transmitted infections, including human papillomavirus (HPV). Patients infected with carcinogenic strains of HPV (ie, 16, 18, and 31) are at risk of squamous cell carcinoma of the cervix.

### References

- HPV infection and cervical neoplasia: associated risk factors



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End Block



A 64-year-old woman comes to the office for evaluation of a vulvar lesion. The patient has had a vulvar plaque for the past year that has slowly increased in size. She underwent menopause at age 52 and has a 30-year smoking history. Vital signs are normal. Physical examination shows a 1-cm nonfriable, white plaque on the right labia majora. The remainder of the physical examination is normal. A biopsy of the lesion is performed and shows squamous cell carcinoma. A sentinel lymph node biopsy is planned for cancer staging. This procedure should target which of the following lymph nodes?

- ☐ A. Common iliac
- ☐ B. External iliac
- ☐ C. Inguinofemoral
- ☐ D. Obturator
- ☐ E. Paraaortic
- ☐ F. Presacral

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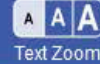
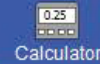
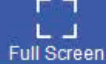
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A 64-year-old woman comes to the office for evaluation of a vulvar lesion. The patient has had a vulvar plaque for the past year that has slowly increased in size. She underwent menopause at age 52 and has a 30-year smoking history. Vital signs are normal. Physical examination shows a 1-cm nonfriable, white plaque on the right labia majora. The remainder of the physical examination is normal. A biopsy of the lesion is performed and shows squamous cell carcinoma. A sentinel lymph node biopsy is planned for cancer staging. This procedure should target which of the following lymph nodes?

- ☐ A. Common iliac (5%)
- ☐ B. External iliac (24%)
- ☒ C. Inguinofemoral (59%)
- ☐ D. Obturator (1%)
- ☐ E. Paraaortic (9%)
- ☐ F. Presacral (0%)





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### Lymph node drainage of the female reproductive system

Uterus	• External iliac
Cervix	• Internal iliac
Vagina	• Proximal: internal iliac • Distal: inguinofemoral
Vulva	• Inguinofemoral
Ovaries	• Paraaortic

This patient has **squamous cell carcinoma** (SCC), the most common type of **vulvar cancer**. Patients with vulvar cancer typically present with either an ulcerative lesion or plaque on the labia. Risk factors include chronic human papillomavirus infection, prior vulvar lichen sclerosus, and tobacco use.

Like most carcinomas, vulvar carcinoma can spread directly to adjacent structures (eg, perineum, vagina) or from the primary site to regional lymph nodes via lymphatic drainage. Therefore, initial cancer staging typically assesses for tumor spread in the first lymph nodes to drain the primary tumor site (ie, **sentinel lymph node biopsy**) because they are the most likely to have tumor involvement. The lymphatic drainage



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**lymph node biopsy**) because they are the most likely to have tumor involvement. The lymphatic drainage of the vulva is initially to the **inguinofemoral nodes**, which consists of a superficial inguinal and a deeper femoral node.

**(Choices A and B)** Lymph from the uterine corpus and inguinal nodes (which drain the lower extremities, buttocks, and external genitalia) subsequently drain to the external iliac nodes. The external iliac nodes and internal iliac nodes both drain to the common iliac nodes.

**(Choice D)** The bladder, uterus, and cervix can drain to the obturator nodes, which are located in the obturator fossa medial to the external iliac vessels. The obturator nodes are 1 of 3 pelvic lymph node groups (ie, obturator, external iliac, internal iliac) that together drain the pelvis, lower extremities, and lower abdominal wall.

**(Choice E)** Lymph from the ovary and common iliac node drain to the paraaortic lymph nodes.

**(Choice F)** The anal canal and rectum drain to the presacral lymph nodes.

### **Educational objective:**

Squamous cell carcinoma of the vulva can metastasize via lymphatic drainage. The vulva first drains to the inguinofemoral nodes of the groin, which should be the target for sentinel lymph node biopsy because they are the most likely lymph nodes to have tumor involvement.



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Feedback

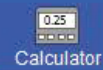
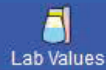


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A 49-year-old woman, gravida 2, para 2, comes to the office due to 10 months of irregular vaginal bleeding. Her last menstrual period was 3 years ago. She has a history of hypothyroidism and takes levothyroxine daily. Ultrasound reveals a thickened endometrium and a solid left adnexal mass. Endometrial biopsy is abnormal, and the patient requires surgery. Intraoperatively, the ovarian mass is yellow and firm. Pathology reports small cuboidal cells in sheets with gland-like structures containing acidophilic material. The cells are arranged in a microfollicular pattern around a pink, eosinophilic center. Which of the following is most likely secreted by this patient's tumor?

- ☐ A.  $\alpha$ -fetoprotein
- ☐ B.  $\beta$ -hCG
- ☐ C. CA-125
- ☐ D. Estrogen
- ☐ E. Testosterone
- ☐ F. Thyroxine





bleeding. Her last menstrual period was 3 years ago. She has a history of hypothyroidism and takes levothyroxine daily. Ultrasound reveals a thickened endometrium and a solid left adnexal mass. Endometrial biopsy is abnormal, and the patient requires surgery. Intraoperatively, the ovarian mass is yellow and firm. Pathology reports small cuboidal cells in sheets with gland-like structures containing acidophilic material. The cells are arranged in a microfollicular pattern around a pink, eosinophilic center. Which of the following is most likely secreted by this patient's tumor?

- ☐ A.  $\alpha$ -fetoprotein (15%)
- ☐ B.  $\beta$ -hCG (9%)
- ☐ C. CA-125 (23%)
- ☒ D. Estrogen (38%)
- ☐ E. Testosterone (1%)
- ☐ F. Thyroxine (11%)

Correct

38%



58 secs



02/01/2021

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Granulosa cell tumor of the ovary	
Clinical features	<ul style="list-style-type: none"><li>• Large, unilateral adnexal mass</li><li>• ↑ Estrogen (endometrial hyperplasia, precocious puberty)</li><li>• ↑ Inhibin</li></ul>
Histology	<ul style="list-style-type: none"><li>• Call-Exner bodies (cuboidal granulosa cells in a rosette pattern with coffee bean nuclei)</li><li>• Yellow theca cells with lipid</li></ul>

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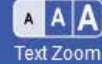
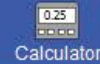
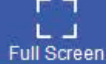
**Granulosa cell tumors** comprise approximately 5% of all ovarian tumors and are primarily identified in **postmenopausal** women. These tumors are derived from the ovarian stroma and are classified as **sex cord-stromal tumors**, which contain a predominance of granulosa cells and a scattering of theca cells. The granulosa cells are small and cuboidal in shape, grow in cords or sheets, and form follicle- or rosette-like structures (**Call-Exner bodies**) that have a gland-like appearance with a pink eosinophilic center and **coffee bean nuclei** (black arrows). Theca cells are plump with lipid contents, which give the mass a yellow color on gross inspection.



Exhibit Display



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color on gross inspection.

Typically, granulosa-theca cell tumors are **unilateral** and large. Unlike epithelial ovarian cancers, these masses **secrete estrogen** and can present with **endometrial hyperplasia** (eg, postmenopausal bleeding with thickened endometrium on ultrasound). The unopposed estrogen leads to hyperplasia of the endometrial cells and glands, and the increased cellular division of the hyperplastic cells in turn increases the risk of cellular atypia and endometrial carcinoma. In young patients, excessive estrogen levels may cause precocious sexual development.

**(Choice A)**  $\alpha$ -fetoprotein (AFP) is normally produced by the fetal liver and yolk sac, but it can also be used as a tumor marker in patients with hepatocellular, nonseminomatous testicular, or ovarian carcinomas.

**(Choice B)**  $\beta$ -hCG is used to confirm pregnancy and screen for gestational trophoblastic disease and germ cell tumors.

**(Choice C)** Cancer antigen 125 (CA-125) is elevated in epithelial carcinomas of the ovary (eg, serous, endometrioid, clear cell). Stromal tumors do not release significant amounts of CA-125.

**(Choice E)** Testosterone is produced by Sertoli-Leydig tumors, another type of ovarian sex cord tumor. Affected patients present with evidence of hyperandrogenism (eg, hirsutism, clitoromegaly, deepening voice).





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**(Choice C)** Cancer antigen 125 (CA-125) is elevated in epithelial carcinomas of the ovary (eg, serous, endometrioid, clear cell). Stromal tumors do not release significant amounts of CA-125.

**(Choice E)** Testosterone is produced by Sertoli-Leydig tumors, another type of ovarian sex cord tumor. Affected patients present with evidence of hyperandrogenism (eg, hirsutism, clitoromegaly, deepening voice).

**(Choice F)** Struma ovarii is a germ cell tumor of the ovary that can cause hyperthyroidism by secreting thyroxine. Histopathology of this tumor reveals mature thyroid tissue.

### Educational objective:

Granulosa cell tumors are sex-cord stromal tumors of the ovary that secrete estrogen and can cause endometrial hyperplasia. Call-Exner bodies (cells arranged in a microfollicular or rosette pattern) are seen on microscopy. On gross pathology, the tumor appears yellow due to the lipid content in theca cells.

### References

- [Pathology of the adnexal mass.](#)

Pathology

Female Reproductive System &amp; Breast

Ovarian cancer

Subject

System

Topic



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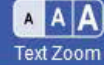
Notes



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Settings

A 29-year-old nulliparous woman comes to the emergency department with right-sided pelvic pain. The pain is sharp and came on suddenly while she was shoveling snow this morning. It is accompanied by nausea and is worse with movement. The patient's last menstrual period was 2 weeks ago. Her temperature is 37.8 C (100 F), blood pressure is 100/60 mm Hg, and pulse is 92/min. Pelvic ultrasound reveals a normal-sized uterus and left ovary, and a right adnexal mass measuring 6 cm with no blood flow to the ovary. Urine  $\beta$ -hCG is negative. The patient's condition most likely involves pathology in which of the following structures?

- ☐ A. Broad ligament
- ☐ B. Infundibulopelvic ligament
- ☐ C. Mesosalpinx
- ☐ D. Round ligament
- ☐ E. Uterosacral ligament

**Submit**

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A 29-year-old nulliparous woman comes to the emergency department with right-sided pelvic pain. The pain is sharp and came on suddenly while she was shoveling snow this morning. It is accompanied by nausea and is worse with movement. The patient's last menstrual period was 2 weeks ago. Her temperature is 37.8 C (100 F), blood pressure is 100/60 mm Hg, and pulse is 92/min. Pelvic ultrasound reveals a normal-sized uterus and left ovary, and a right adnexal mass measuring 6 cm with no blood flow to the ovary. Urine  $\beta$ -hCG is negative. The patient's condition most likely involves pathology in which of the following structures?

- ☐ A. Broad ligament (14%)
- ☒ B. Infundibulopelvic ligament (45%)
- ☐ C. Mesosalpinx (14%)
- ☐ D. Round ligament (22%)
- ☐ E. Uterosacral ligament (1%)





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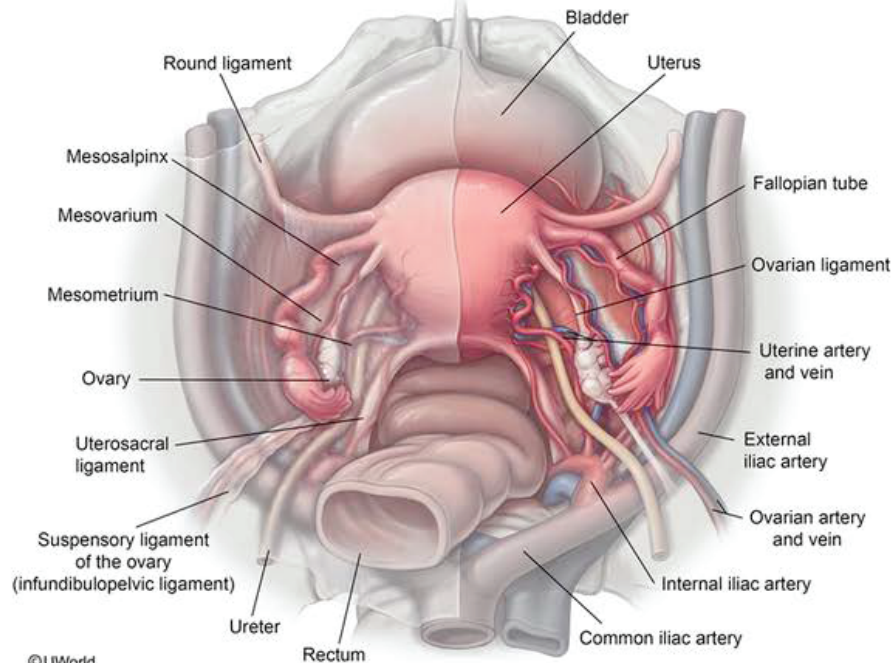
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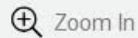
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## Exhibit Display

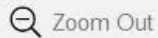
## Surgeon's view (superior view) of the female pelvis



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The ovary is suspended posterolaterally to the uterus by the utero-ovarian ligament and receives its blood supply through the vessels that traverse the **infundibulopelvic (IP) ligament (eg, suspensory ligament of the ovary)**. The IP ligament also houses the ovarian nerve plexus. Rotation of the ovary around the IP ligament results in **ovarian torsion**.

The main risk factor for torsion is the presence of a large ovarian mass (eg, cyst, neoplasm). The weight of the mass causes the ovary to **twist** and **occlude the ovarian vessels and nerves**. When blood flow to the ovary is completely blocked, the torsed ovary becomes **edematous and ischemic**. A patient with ovarian torsion will typically present with sudden-onset **unilateral pelvic pain** and nausea and sometimes vomiting and fever. Pelvic ultrasound is the first-line diagnostic test and may show decreased or no blood flow to the ovary.

**(Choices A and C)** The mesosalpinx is the portion of the broad ligament that connects the fallopian tubes to the pelvic sidewall. The broad ligament is a wide sheet of peritoneal tissue that encapsulates the reproductive organs anteriorly and posteriorly and attaches the uterus to the pelvic sidewalls bilaterally, making torsion of the ovary around the broad ligament (including mesosalpinx) anatomically impossible.

**(Choice D)** The round ligament maintains the anteflexion of the uterus. It runs from the lower aspect of the uterus through the inguinal ring to the labia majora and is not connected to the ovaries. During



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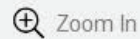
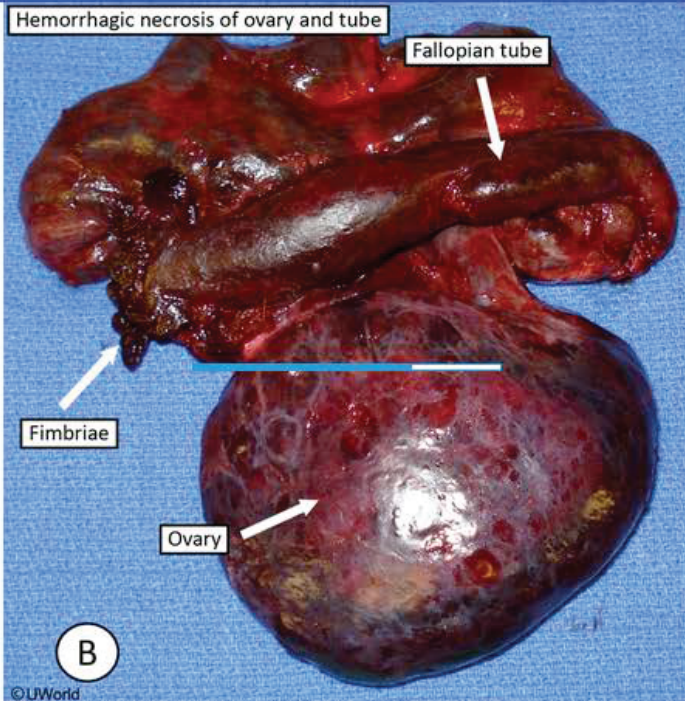


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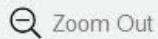


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**(Choice D)** The round ligament maintains the antelexion of the uterus. It runs from the lower aspect of the uterus through the inguinal ring to the labia majora and is not connected to the ovaries. During pregnancy, a woman may experience intermittent sharp pain due to irritation from sudden movements of the stretching round ligament.

**(Choice E)** The uterosacral ligaments connect the posterior aspect of the uterus to the anterior portion of the sacrum. These ligaments hold the uterus in an anteverted or retroverted position; loss of this support contributes to uterine prolapse into the vagina. They are not involved in the positioning or vascular supply of the ovaries.

### Educational objective:

Ovarian torsion typically involves twisting of the infundibulopelvic ligament, often due to the weight of a large adnexal mass. The resulting occlusion of the blood and nerve supply to the ovary results in severe, acute pelvic pain and ovarian ischemia.

### References

- [Clinical risk factors for ovarian torsion.](#)

Anatomy

Female Reproductive System &amp; Breast

Ovarian Torsion

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Settings

A 61-year-old woman comes to the office due to skin dimpling on the right breast. She first noticed the skin changes 3 months ago while on vacation and is concerned that they have not resolved. The patient does not use tobacco, alcohol, or illicit drugs. She exercises regularly and takes a daily multivitamin. Her last menstrual period was 8 years ago. Physical examination shows a prominent, nontender skin retraction without discoloration or swelling of the right breast. There is also a 6-cm irregular, immobile, firm mass in the right upper outer quadrant of the breast. The left breast appears normal. This patient's skin findings are likely due to malignant infiltration of which of the following structures?

- ☐ A. Axillary lymph nodes
- ☐ B. Lactiferous ducts
- ☐ C. Mammary vein
- ☐ D. Nipple
- ☐ E. Suspensory ligaments

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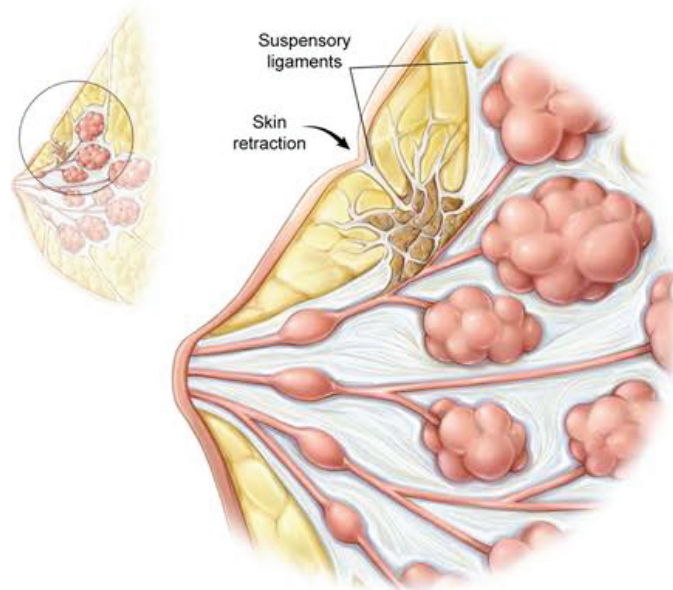
A 61-year-old woman comes to the office due to **skin dimpling** on the right breast. She first noticed the skin changes 3 months ago while on vacation and is concerned that they have not resolved. The patient does not use tobacco, alcohol, or illicit drugs. She exercises regularly and takes a daily multivitamin. Her last menstrual period was 8 years ago. Physical examination shows a prominent, nontender skin retraction without discoloration or swelling of the right breast. There is also a 6-cm irregular, immobile, firm mass in the right upper outer quadrant of the breast. The left breast appears normal. This patient's skin findings are likely due to malignant infiltration of which of the following structures?

- ☐ A. Axillary lymph nodes (12%)
- ☐ B. Lactiferous ducts (15%)
- ☐ C. Mammary vein (0%)
- ☐ D. Nipple (1%)
- ☒ E. Suspensory ligaments (69%)



### Exhibit Display

#### Breast cancer spread to suspensory ligament



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Settings

Breast cancer is the most commonly diagnosed malignancy in women in the United States and the second most common cause of cancer death in women. **Invasive breast carcinoma** typically presents as an irregularly shaped, adherent breast mass. The upper outer quadrants of the breast are the most common site of breast cancer. Overlying **skin retractions** (puckering) signal involvement of **suspensory ligaments** of the breast (ie, **Cooper ligaments**). Malignant infiltration of these ligaments causes fibrosis and shortening, leading to traction on the skin with distortion in breast contour.

**(Choice A)** Axillary lymph nodes are the most common site of metastasis for breast cancer. As malignant cells spread through the lymphatics, they can block cutaneous lymphatic flow, causing peau d'orange (thickened, dimpled skin like an orange peel). However, this finding is distinct from skin retractions and is associated with discoloration and swelling of the breast.

**(Choices B and D)** Lactiferous ducts connect the nipple to the mammary lobules to allow lactation. Malignant spread of ductal carcinoma through the ductal system may cause nipple discharge, whereas spread to the nipple surface causes **Paget disease** of the nipple (eg, eczematous exudate over the nipple and areola).

**(Choice C)** The internal mammary vein runs along the thoracic lymphatics, draining the medial portions of the breast, and may be a site of metastasis from lesions in that area. Spread to the vasculature often



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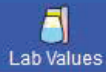
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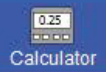
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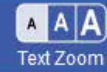
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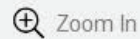
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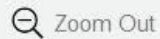
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Breast cancer is the most commonly diagnosed malignancy in women in the United States and the second

### Exhibit Display



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Settings

Malignant spread of ductal carcinoma through the ductal system may cause nipple discharge, whereas spread to the nipple surface causes **Paget disease** of the nipple (eg, eczematous exudate over the nipple and areola).

**(Choice C)** The internal mammary vein runs along the thoracic lymphatics, draining the medial portions of the breast, and may be a site of metastasis from lesions in that area. Spread to the vasculature often results in distant hematogenous metastasis.

### Educational objective:

Invasive breast carcinoma typically presents as an irregularly shaped, adherent breast mass, most commonly in the upper outer quadrant. Malignant infiltration of suspensory ligaments of the breast can cause skin retractions.

### References

- [Breast anatomy for the interventionalist.](#)

Anatomy

Female Reproductive System &amp; Breast

Breast cancer

Subject

System

Topic

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Settings

A 29-year-old woman, gravida 2, para 2, comes to the emergency department with fever, crampy abdominal pain, and right flank pain 8 days after an uncomplicated vaginal delivery. Her temperature is 38.3 C (101 F) and blood pressure is 110/60 mm Hg. A physical examination shows tenderness in the right lower quadrant and flank. She is hospitalized and given intravenous antibiotics for a presumed uterine infection, but her fever persists. Urine and blood cultures show no bacterial growth. A CT scan of her abdomen and pelvis reveals right ovarian vein thrombosis. If this patient remains untreated, she is at risk for extension of the thrombus into which of the following veins?

- ☐ A. Inferior vena cava
- ☐ B. Right common iliac vein
- ☐ C. Right internal iliac vein
- ☐ D. Right renal vein
- ☐ E. Right uterine vein

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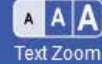
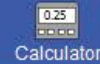
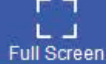
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- ☒ A. Inferior vena cava (70%)
- ☐ B. Right common iliac vein (3%)
- ☐ C. Right internal iliac vein (16%)
- ☐ D. Right renal vein (8%)
- ☐ E. Right uterine vein (2%)





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Settings

### Postpartum ovarian vein thrombosis

#### Risk factors

- Venous stasis (ovarian venous dilation)
- Hypercoagulability (hormonally-mediated increase in clotting factors)
- Endothelial damage (intrapartum vascular injury)

#### Clinical features

- Persistent fever after delivery
- Localized abdominal/flank pain
- No response to antibiotics

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Thrombosis risk is markedly increased during pregnancy and puerperium due to **Virchow's triad**:

- Stasis from pregnancy-related venous dilation and compression of the inferior vena cava (IVC) and iliac veins by the gravid uterus
- Physiologic increases in factors VII, VIII, and X, as well as von Willebrand factor and fibrinogen (to protect from hemorrhage during miscarriage or childbirth)
- Endothelial damage due to uterine infection or intrapartum vascular trauma



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Thrombosis risk is markedly increased during pregnancy and puerperium due to **Virchow's triad**:

- Stasis from pregnancy-related venous dilation and compression of the inferior vena cava (IVC) and iliac veins by the gravid uterus
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- Endothelial damage due to uterine infection or intrapartum vascular trauma

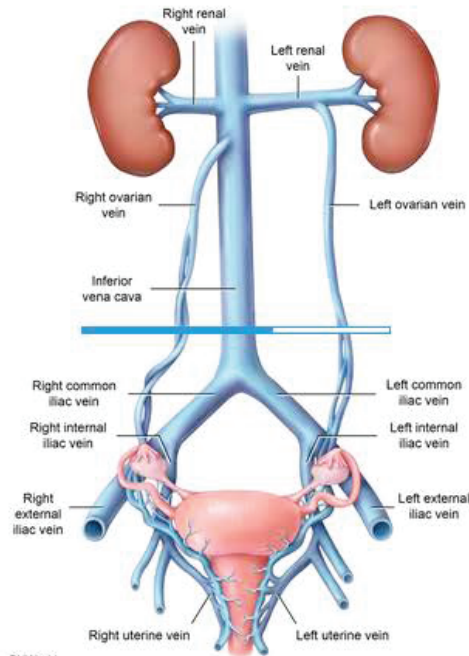
**Ovarian vein thrombosis** is an example of septic pelvic thrombophlebitis, a complication that can occur via vaginal or cesarean delivery. Patients with ovarian vein thrombosis typically present with **fever** and **localized abdominal pain** one week after delivery and are usually hospitalized for a presumed uterine infection. When fever persists despite antibiotics, a CT or MRI scan can confirm the presence of a thrombus in the ovarian vein.

**Ovarian venous drainage** is asymmetric; the **left ovarian vein** drains into the **left renal vein (Choice D)** while the **right ovarian vein** drains directly into the **IVC**, and a clot can potentially extend into the IVC. Ovarian vein thrombosis is more commonly right-sided, but pulmonary emboli are uncommon and morbidity/mortality is low.



### Exhibit Display

#### Venous drainage of the female pelvis



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Ovarian vein thrombosis is more commonly right-sided, but pulmonary emboli are uncommon and morbidity/mortality is low.

**(Choices B and C)** In pregnancy, venous stasis and hypercoagulability predispose patients to proximal vein thrombosis (involving the iliac, femoral, or deep popliteal veins), which carries a risk of embolization into the pulmonary circulation. As the ovarian vasculature does not drain into the iliac vessels, there is no risk for clot extension to the common or internal iliac veins.

**(Choice E)** The uterine vein drains into the internal iliac vein. Extension of the clot to the uterine veins would require that the clot extend through the uterine venous plexus, which is less likely than direct extension through the ovarian vein toward the IVC.

### Educational objective:

Venous stasis and hypercoagulability from pregnancy in addition to endothelial damage from delivery can cause ovarian vein thrombosis in the puerperium. Symptoms include fever and localized abdominal or flank pain. Most thrombosis is right-sided and can extend to the inferior vena cava; however, left ovarian vein thrombosis can extend to the left renal vein.

### References

- [Ovarian vein thrombosis.](#)







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Settings

A 14-year-old girl is brought to the physician for a routine checkup. When asked about her menstrual periods, she says that she does not get them every month. When she does have her period, she bleeds for 7-10 days and needs to use nearly twice as many tampons a day as her older sister. She also complains of occasional spotting that happens outside of her normal periods. The patient underwent menarche a year ago and her last period was 6 weeks ago. She eats a balanced diet and exercises 3 times a week with her volleyball team. Her past medical history is unremarkable, and her body mass index is 25 kg/m<sup>2</sup>. Which of the following is the most likely cause of this patient's complaints?

- ☐ A. Anovulatory cycles
- ☐ B. Complex atypical hyperplasia of the endometrium
- ☐ C. Endometrial atrophy
- ☐ D. Endometrial stimulation by progesterone
- ☐ E. Increased follicle-stimulating hormone secretion

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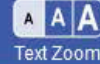
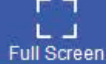
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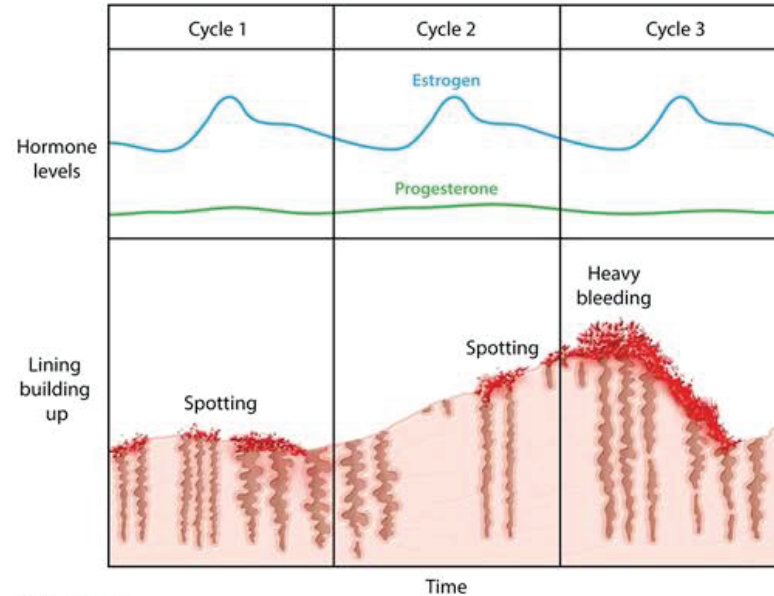
- ☒ A. Anovulatory cycles (76%)
- ☐ B. Complex atypical hyperplasia of the endometrium (9%)
- ☐ C. Endometrial atrophy (1%)
- ☐ D. Endometrial stimulation by progesterone (5%)
- ☐ E. Increased follicle-stimulating hormone secretion (6%)



## Effects of anovulatory cycles on the endometrium

### Exhibit Display

### Effects of anovulatory cycles on the endometrium



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In most women age 20-40 years, menstrual cycles are consistent and last 24-35 days, with menstrual flow ranging from 4-6 days. However, adolescents typically have an immature hypothalamic-pituitary-ovarian axis for several years following menarche. During this time, they may have longer menstrual cycles and irregular bleeding patterns due to the presence of anovulatory cycles. In the absence of ovulation, the ovarian follicle does not degenerate and become a corpus luteum. As a result, no progesterone is produced and estrogen levels remain persistently high, causing the endometrium to remain in the proliferative phase. Chronically proliferative endometrium becomes disorganized and fragile with unstable venous capillaries, resulting in irregular periods of stromal breakdown with variable, but often heavy, bleeding.

By young adulthood, ovulation occurs regularly and menstrual cycles become more predictable. However, as women approach menopause in their late 40s, anovulation becomes more prevalent and menstrual irregularity ensues.

**(Choice B)** Complex atypical hyperplasia of the endometrium is associated with prolonged exposure to estrogen without opposing progesterone, which may develop from chronic anovulation over many years. This condition is most common in obese older women or those who receive estrogen without progesterone during hormone replacement therapy.



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Settings

estrogen without opposing progesterone, which may develop from chronic anovulation over many years.

This condition is most common in obese older women or those who receive estrogen without progesterone during hormone replacement therapy.

**(Choice C)** Endometrial atrophy is an expected finding in post-menopausal women or women using certain types of hormonal contraception. Endometrial atrophy can cause intermittent spotting.

**(Choice D)** In a **normal ovulatory cycle**, estrogen stimulates endometrial proliferation and progesterone stimulates endometrial secretory changes in preparation for implantation. When estrogen and progesterone levels drop toward the end of the cycle, the loss of trophic stimulus causes the endometrium to degenerate, resulting in menstrual bleeding.

**(Choice E)** Increased follicle-stimulating hormone secretion occurs in post-menopausal women or in premature ovarian failure when ovaries no longer produce the estrogen that provides normal negative feedback to the pituitary gland.

### Educational objective:

Anovulation is common in the first several years after menarche and the last few years before menopause. It manifests with marked menstrual cycle variability.



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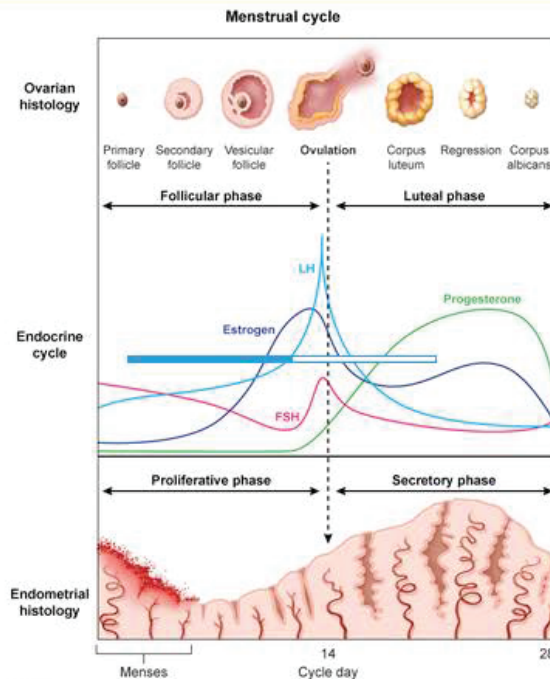
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estrogen without opposing progesterone, which may develop from chronic anovulation over many years.

### Exhibit Display



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Settings

A 42-year-old woman, gravida 4 para 4, comes to the office due to heavy and painful menstrual bleeding over the past 3 months. The patient's last menstrual period was 3 weeks ago. Menarche was at age 10, and menstrual periods last for 3-5 days and occur every 30 days. She is sexually active with her husband and does not have pain with intercourse. The patient had a bilateral tubal ligation 3 years ago after the birth of her last child. She takes no medications and has no allergies. BMI is 24 kg/m<sup>2</sup>. Vital signs are normal. On bimanual examination, the uterus is uniformly enlarged and tender. Urine  $\beta$ -hCG is negative. Which of the following is the most likely cause of this patient's symptoms?

- ☐ A. Benign myometrial smooth muscle cell proliferation
- ☐ B. Blastocyst implantation in the fallopian tube
- ☐ C. Endometrial glands and stroma within the myometrium
- ☐ D. Localized overgrowth of endometrium into the uterine cavity
- ☐ E. Unregulated endometrial proliferation with increased gland-to-stroma ratio

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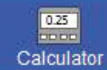
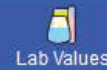
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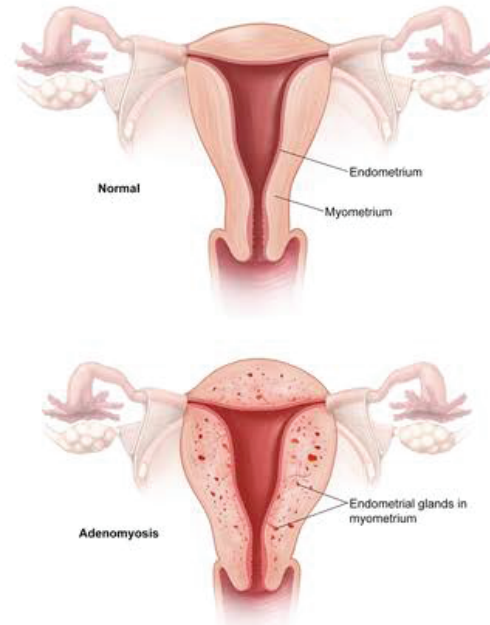
A 42-year-old woman, gravida 4 para 4, comes to the office due to heavy and painful menstrual bleeding over the past 3 months. The patient's last menstrual period was 3 weeks ago. Menarche was at age 10, and menstrual periods last for 3-5 days and occur every 30 days. She is sexually active with her husband and does not have pain with intercourse. The patient had a bilateral tubal ligation 3 years ago after the birth of her last child. She takes no medications and has no allergies. BMI is 24 kg/m<sup>2</sup>. Vital signs are normal. On bimanual examination, the uterus is uniformly enlarged and tender. Urine  $\beta$ -hCG is negative. Which of the following is the most likely cause of this patient's symptoms?

- ☐ A. Benign myometrial smooth muscle cell proliferation (20%)
- ☐ B. Blastocyst implantation in the fallopian tube (1%)
- ☒ C. Endometrial glands and stroma within the myometrium (48%)
- ☐ D. Localized overgrowth of endometrium into the uterine cavity (10%)
- ☐ E. Unregulated endometrial proliferation with increased gland-to-stroma ratio (19%)



### Exhibit Display

Normal uterus vs adenomyosis



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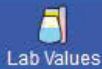
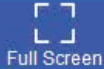
This patient has **adenomyosis**, a disorder caused by an abnormal collection of **endometrial glands and stroma within the uterine myometrium**. Adenomyosis is common in multiparous women, and prior uterine surgery (eg, cesarean delivery) is a risk factor.

Although the exact pathogenesis is unclear, adenomyosis may occur due to endometrial invagination into the myometrium during periods of myometrial weakening or changes in vascularity at the endomyometrial interface (eg, pregnancy, uterine surgery). The clinical features of adenomyosis reflect its pathophysiology:

- endometrial gland proliferation and cyclic bleeding within the myometrium leads to **dysmenorrhea** and **uterine tenderness**
- abnormal myometrial hyperplasia and hypertrophy results in a concentric, **uniformly enlarged uterus**
- uterine enlargement and subsequently increased endometrial surface area causes **regular, heavy menstrual bleeding**

Definitive therapy is with hysterectomy, which allows for histologic diagnosis.

**(Choice A)** Leiomyomas (ie, uterine fibroids) are benign myometrial smooth muscle cell tumors. Although fibroids can cause regular, heavy menses (also due to increased endometrial surface area), the uterus is



**(Choice A)** Leiomyomas (ie, uterine fibroids) are benign myometrial smooth muscle cell tumors. Although fibroids can cause regular, heavy menses (also due to increased endometrial surface area), the uterus is typically nontender and **irregularly enlarged** rather than tender and uniformly enlarged.

**(Choice B)** An **ectopic pregnancy** most commonly occurs due to abnormal blastocyst implantation in the fallopian tube. Although prior tubal surgery (eg, bilateral tubal ligation) is a risk factor, ectopic pregnancy is unlikely in this patient with a negative urine  $\beta$ -hCG. In addition, uterine enlargement would not be seen.

**(Choice D)** **Endometrial polyps** are benign, intracavitary, focal hyperplastic growths of endometrial tissue. In contrast to adenomyosis, endometrial polyps cause painless intermenstrual bleeding rather than painful, cyclic, heavy menses. There is also no associated uterine tenderness or enlargement.

**(Choice E)** Patients with endometrial hyperplasia have unregulated endometrial gland proliferation with increased gland-to-stroma ratio; the thickened endometrial lining may slightly increase uterine size and cause heavy menses. However, endometrial hyperplasia does not typically cause dysmenorrhea or uterine tenderness. In addition, the most common risk factor is unopposed estrogen from chronic anovulation and/or obesity; this patient has regular menses and a normal BMI.

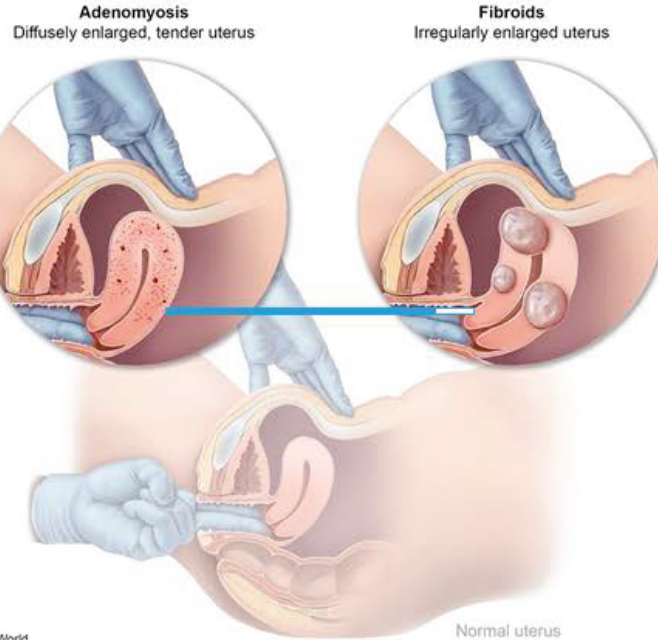
### Educational objective:

Adenomyosis is the abnormal presence of endometrial glands and stroma within the uterine myometrium.



### Exhibit Display

#### Adenomyosis vs fibroids

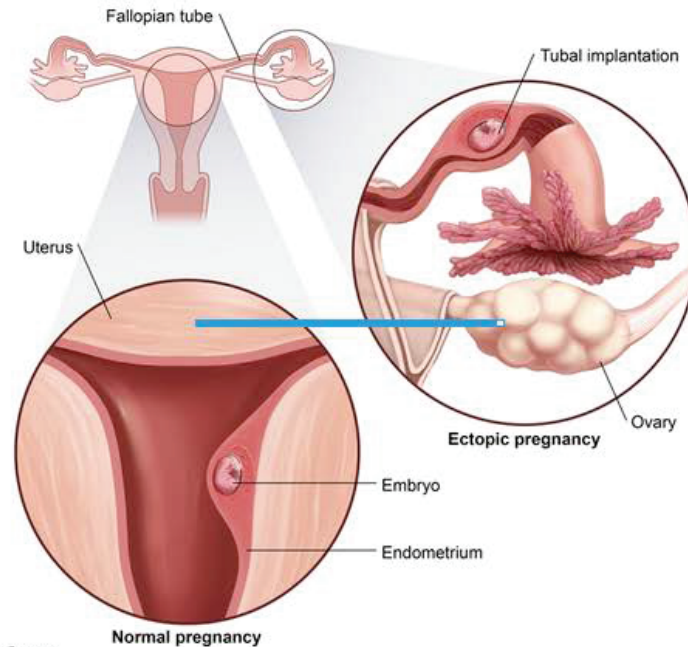


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### Exhibit Display

#### Ectopic pregnancy



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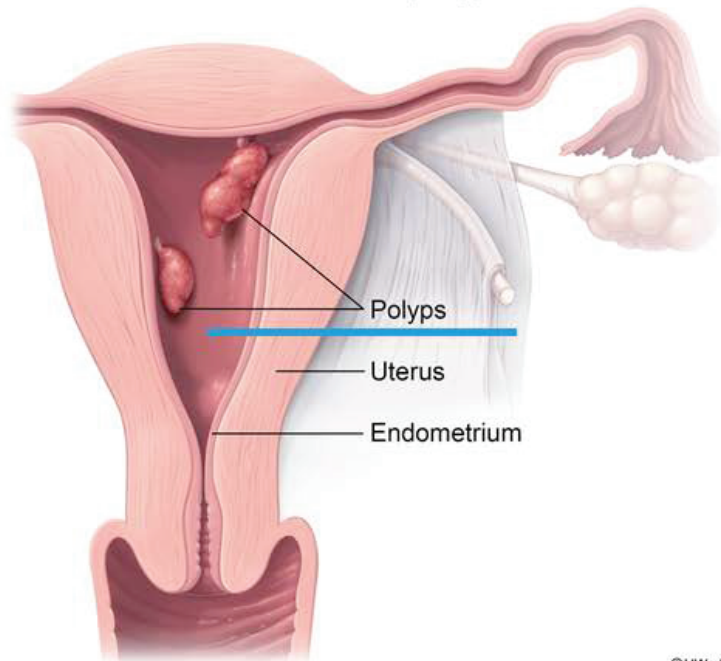
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### Exhibit Display

## Endometrial polyps



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Adenomyosis is the abnormal presence of endometrial glands and stroma within the uterine myometrium.



unlikely in this patient with a negative urine  $\beta$ -hCG. In addition, uterine enlargement would not be seen.

**(Choice D)** Endometrial polyps are benign, intracavitary, focal hyperplastic growths of endometrial tissue.

In contrast to adenomyosis, endometrial polyps cause painless intermenstrual bleeding rather than painful, cyclic, heavy menses. There is also no associated uterine tenderness or enlargement.

**(Choice E)** Patients with endometrial hyperplasia have unregulated endometrial gland proliferation with increased gland-to-stroma ratio; the thickened endometrial lining may slightly increase uterine size and cause heavy menses. However, endometrial hyperplasia does not typically cause dysmenorrhea or uterine tenderness. In addition, the most common risk factor is unopposed estrogen from chronic anovulation and/or obesity; this patient has regular menses and a normal BMI.

### Educational objective:

Adenomyosis is the abnormal presence of endometrial glands and stroma within the uterine myometrium. Affected patients are typically multiparous women with dysmenorrhea, heavy menses, and a uniformly enlarged uterus.

### References

- Adenomyosis: what is new?







Mark



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Lab Values



Notes



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Text Zoom



Settings

A 21-year-old Caucasian woman comes to the office with facial flushing, headache, nausea, vomiting, and abdominal cramps after drinking alcohol at a party. Approximately 1 week ago, the patient was seen by a health care provider who prescribed a new oral medication. However, the patient cannot recall the name or reason it was prescribed. The patient also takes oral contraceptives and is sexually active with her boyfriend. She smokes cigarettes and drinks alcohol "sometimes." The patient is intoxicated and unable to provide further information. This patient is most likely being treated for which of the following conditions?

- ☐ A. Anxiety
- ☐ B. *Candida* vaginitis
- ☐ C. Deep venous thrombosis
- ☐ D. Menstrual cramps
- ☐ E. Seasonal allergies
- ☐ F. *Trichomonas* vaginitis

**Submit**

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Settings

A 21-year-old Caucasian woman comes to the office with **facial flushing**, headache, nausea, vomiting, and abdominal cramps after drinking alcohol at a party. Approximately 1 week ago, the patient was seen by a health care provider who prescribed a new oral medication. However, the patient cannot recall the name or reason it was prescribed. The patient also takes oral contraceptives and is sexually active with her boyfriend. She smokes cigarettes and drinks alcohol "sometimes." The patient is intoxicated and unable to provide further information. This patient is most likely being treated for which of the following conditions?

- ☐ A. Anxiety (17%)
- ☐ B. *Candida* vaginitis (9%)
- ☐ C. Deep venous thrombosis (3%)
- ☐ D. Menstrual cramps (4%)
- ☐ E. Seasonal allergies (2%)
- ☒ F. *Trichomonas* vaginitis (62%)



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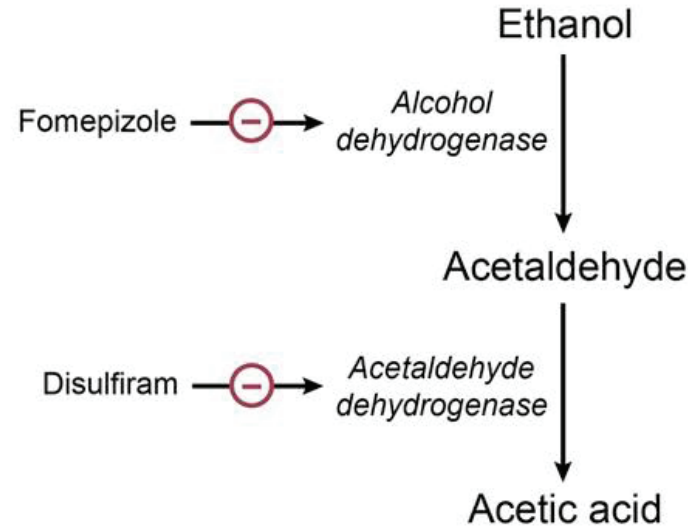
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Exhibit Display

## Alcohol metabolism



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Settings

Medication-alcohol interactions can increase the risk of illness and injury. Patients receiving **metronidazole** can develop a **disulfiram-like reaction** shortly after **ethanol consumption**. Metronidazole is used to treat **trichomonas vaginitis** and **bacterial vaginosis**, and alcohol-containing beverages and medications should be avoided during the treatment course.

Although it is not well tolerated, disulfiram is a medication that can be used in recovering alcoholics to prevent relapse. This drug inhibits acetaldehyde dehydrogenase and causes **acetaldehyde accumulation**. Metronidazole's interaction with alcohol is similar to that with disulfiram, exhibiting comparable systemic adverse effects such as headache, abdominal cramps, nausea, and flushing.

**(Choices A and E)** Benzodiazepines are a treatment option for anxiety. Allergies can be treated with antihistamines. Alcohol use with both of these medication classes is dangerous as it intensifies sedative and depressive effects.

**(Choice B)** *Candida* vaginitis is treated with fluconazole, a fungistatic drug that inhibits ergosterol synthesis in the P450 system of fungi.

**(Choice C)** The combination of oral contraceptive use and smoking increases the risk of thrombosis, especially in women over age 35. Deep venous thrombosis is treated with anticoagulants (eg, warfarin),



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**(Choice C)** The combination of oral contraceptive use and smoking increases the risk of thrombosis, especially in women over age 35. Deep venous thrombosis is treated with anticoagulants (eg, warfarin), and alcohol consumption can alter warfarin's bioavailability and a patient's bleeding or clotting risk.

**(Choice D)** Menstrual cramps are treated with nonsteroidal anti-inflammatory drugs (NSAIDs) or oral contraceptives. NSAIDs inhibit cyclooxygenase and cause gastric bleeding which can be exacerbated by alcohol but do not cause a systemic reaction.

### Educational objective:

Metronidazole is used to treat trichomonal vaginitis and bacterial vaginosis. It can cause disulfiram-like effects (eg, abdominal cramps, nausea, headache) when combined with alcohol due to acetaldehyde accumulation.

### References

- [Vulvovaginitis: screening for and management of trichomoniasis, vulvovaginal candidiasis, and bacterial vaginosis.](#)

Pharmacology  
Subject

Female Reproductive System & Breast  
System

Nitroimidazole antibiotics  
Topic



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A 29-year-old nulliparous woman with HIV comes to the office for her first gynecological examination. The patient acquired HIV from her mother at birth and has been noncompliant with health maintenance visits. Menarche was at age 10, cycles occur every 28 days, and her last menstrual period was 2 weeks ago. The patient has 1 lifetime male partner with whom she has been sexually active for 7 years; they use condoms consistently. Her mother had cervical cancer at age 46 and died of AIDS-related complications at age 48. The patient drinks 3-4 cans of beer each night and does not use tobacco or illicit drugs. Papanicolaou test reveals high-grade cervical dysplasia. Which of the following is the strongest risk factor for cervical dysplasia in this patient?

- ☐ A. Age at first intercourse
- ☐ B. Alcohol consumption
- ☐ C. Early menarche
- ☐ D. Family history of cervical cancer
- ☒ E. Immunosuppression
- ☐ F. Nulliparity



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Menarche was at age 10, cycles occur every 28 days, and her last menstrual period was 2 weeks ago.

The patient has 1 lifetime male partner with whom she has been sexually active for 7 years; they use condoms consistently. Her mother had cervical cancer at age 46 and died of AIDS-related complications at age 48. The patient drinks 3-4 cans of beer each night and does not use tobacco or illicit drugs.

Papanicolaou test reveals high-grade cervical dysplasia. Which of the following is the strongest risk factor for cervical dysplasia in this patient?

- ☐ A. Age at first intercourse (14%)
- ☐ B. Alcohol consumption (0%)
- ☐ C. Early menarche (4%)
- ☐ D. Family history of cervical cancer (15%)
- ☒ E. Immunosuppression (61%)
- ☐ F. Nulliparity (2%)

Correct

61%

53 secs

11/08/2020

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### Risk factors for cervical cancer

- Infection with high-risk HPV strains (eg, 16, 18)
- History of sexually transmitted diseases
- Early onset of sexual activity
- Multiple or high-risk sexual partners
- Immunosuppression
- Oral contraceptive use
- Low socioeconomic status
- Tobacco use

**HPV** = human papillomavirus.

The strongest risk factor for **cervical dysplasia** (also known as cervical intraepithelial neoplasia) and **carcinoma** is infection with **human papillomavirus (HPV) type 16 or 18**. HPV is transmitted primarily through sexual intercourse but can also be spread via skin-to-skin contact. Most invasive cervical cancer specimens and high-grade cervical lesions contain HPV DNA. Other risk factors for cervical dysplasia are listed in the table above.



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listed in the table above.

Cervical cancer is rare in young immunocompetent women as their immune systems can normally combat HPV infection. Approximately 50% of patients with untreated high-grade dysplasia will experience spontaneous regression, whereas only 5% will develop invasive cancer. However, individuals with **HIV** are unable to mount an immune response against HPV due to **immunosuppression** from **T cell deficiency**. Therefore, patients with HIV infection commonly have persistent HPV infection, which allows HPV DNA to become incorporated into the epithelial cells. HIV coinfection may also enhance expression of HPV **viral oncogenes E6 and E7**, leading to cervical dysplasia/cancer. Therefore, patients with HIV require frequent Papanicolaou screening for cervical dysplasia/cancer.

**(Choice A)** Women who have intercourse before age 18 have twice the risk of cervical cancer compared to women who have initial intercourse after age 21.

**(Choice B)** Alcohol consumption increases the risk of breast cancer but is not associated with cervical cancer. However, tobacco use is a significant risk factor for cervical cancer.

**(Choice C)** Age at menarche does not affect cervical cancer risk. However, women with menarche before age 12 are at increased risk for breast and endometrial cancers.

**(Choice D)** Family history of cervical cancer is not a risk factor for cervical dysplasia/cancer. There is no



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cancer. However, tobacco use is a significant risk factor for cervical cancer.

**(Choice C)** Age at menarche does not affect cervical cancer risk. However, women with menarche before age 12 are at increased risk for breast and endometrial cancers.

**(Choice D)** Family history of cervical cancer is not a risk factor for cervical dysplasia/cancer. There is no genetic component to cervical dysplasia/cancer as the majority of cervical dysplasias and cancers are caused by HPV, and HPV is a predominantly sexually transmitted infection.

**(Choice F)** Parity does not affect cervical cancer risk. Anovulatory cycles in nulliparous women increase the risk of endometrial cancer.

### Educational objective:

Human papillomavirus (HPV) infection, especially with strain 16 or 18, is the strongest risk factor for development of cervical dysplasia and invasive cervical carcinoma. HIV coinfection allows HPV infection to persist and enhances expression of HPV oncogenes, increasing the risk for cervical dysplasia/cancer.

### References

- Evidence for frequent regression of cervical intraepithelial neoplasia-grade 2.
- ACOG Practice Bulletin No. 131: screening for cervical cancer.



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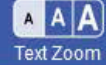
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Settings

A 28-year-old nulliparous woman comes to the clinic to be evaluated for infertility. She has been having unprotected intercourse with her husband for the past 12 months and experiences pain with deep vaginal penetration. Menarche was at age 11 and her period occurs every 26 days and lasts 5-7 days. Her menstrual cycles are accompanied by moderate to severe lower abdominal pain. Pelvic examination shows a normal-sized, retroverted uterus. The posterior vaginal fornix is very tender to palpation. This patient's condition most likely involves which of the following?

- ☐ A. Ectopic endometrial tissue
- ☐ B. Glycogen deficient vaginal epithelium
- ☐ C. Increased endometrial gland to stroma ratio
- ☐ D. Multiple ovarian cysts with cortical fibrosis
- ☐ E. Proliferation of endometrial glands within the myometrium

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Settings

A 28-year-old nulliparous woman comes to the clinic to be evaluated for infertility. She has been having unprotected intercourse with her husband for the past 12 months and experiences pain with deep vaginal penetration. Menarche was at age 11 and her period occurs every 26 days and lasts 5-7 days. Her menstrual cycles are accompanied by moderate to severe lower abdominal pain. Pelvic examination shows a normal-sized, retroverted uterus. The posterior vaginal fornix is very tender to palpation. This patient's condition most likely involves which of the following?

- ☒ A. Ectopic endometrial tissue (66%)
- ☐ B. Glycogen deficient vaginal epithelium (5%)
- ☐ C. Increased endometrial gland to stroma ratio (5%)
- ☐ D. Multiple ovarian cysts with cortical fibrosis (4%)
- ☐ E. Proliferation of endometrial glands within the myometrium (18%)

Correct

 66%  
Answered correctly 48 secs  
Time Spent 12/13/2020  
Last Updated

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## Explanation

Causes of abnormal menstrual bleeding	
Diagnosis	Clinical features
Fibroids	<ul style="list-style-type: none"><li>• Heavy menses</li><li>• Constipation, urinary frequency, pelvic pain/heaviness</li><li>• Enlarged uterus</li></ul>
Adenomyosis	<ul style="list-style-type: none"><li>• Dysmenorrhea, pelvic pain</li><li>• Heavy menses</li><li>• Bulky, globular &amp; tender uterus</li></ul>
Endometrial cancer/hyperplasia	<ul style="list-style-type: none"><li>• History of obesity, nulliparity, or chronic anovulation</li><li>• Irregular, intermenstrual, or postmenopausal bleeding</li><li>• Nontender uterus</li></ul>

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Endometriosis (or ectopic endometrium) refers to the presence of endometrial tissue outside the uterus.

Nulliparity, early menarche, and prolonged menses are risk factors for endometriosis. In contrast,



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**Endometriosis (or ectopic endometrium)** refers to the presence of endometrial tissue outside the uterus.

Nulliparity, early menarche, and prolonged menses are risk factors for endometriosis. In contrast, multiparity, extended lactation, and late menarche decrease the risk due to less frequent menstrual cycles and opportunity for endometrial cells to be disseminated outside the uterus.

Ectopic endometrium responds to hormonal influences of the **menstrual cycle** in the same way as uterine endometrium. Bleeding and shedding of extrauterine endometrium leads to formation of blood collections in the ectopic locations. Over time, the blood undergoes hemolysis and induces inflammation. Local inflammation is followed by adhesion formation, which in turn distorts organ structure and function.

**Adhesions** may interfere with ovulation and fallopian tube function, resulting in **infertility**. Implants and adhesions involving the uterosacral ligament can result in a **fixed, retroverted uterus**. Infiltration of the posterior cul-de-sac can result in **painful intercourse** and tenderness with palpation of the posterior vaginal fornix. Shedding of the ectopic tissue causes **dysmenorrhea** (painful menses).

**(Choice B)** Estrogen deficiency from premature ovarian failure or menopause can result in glycogen deficiency in the vaginal epithelium. The resulting flattening of the labial folds and vaginal rugae can cause dyspareunia. However, this patient's regular menstrual periods reflect normal estrogen levels.

**(Choice C)** Endometrial hyperplasia is characterized by an increased endometrial gland to stroma ratio.



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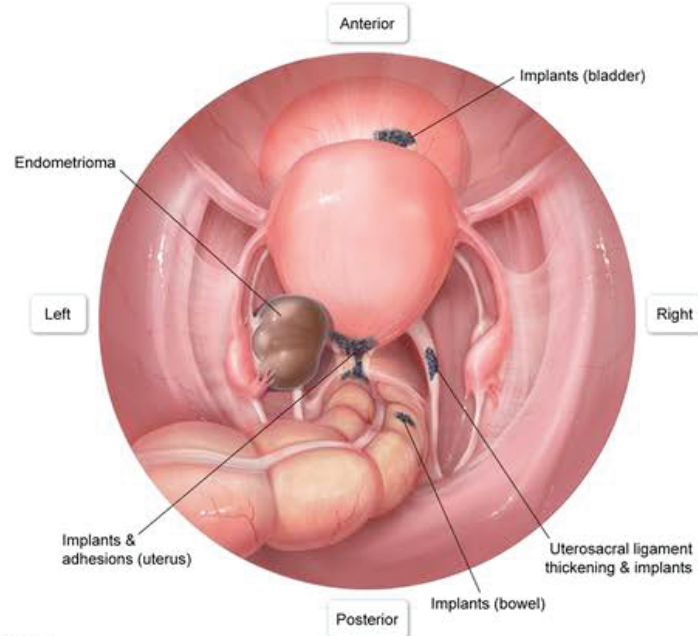
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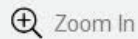
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## Exhibit Display

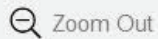
## Pelvic endometriosis



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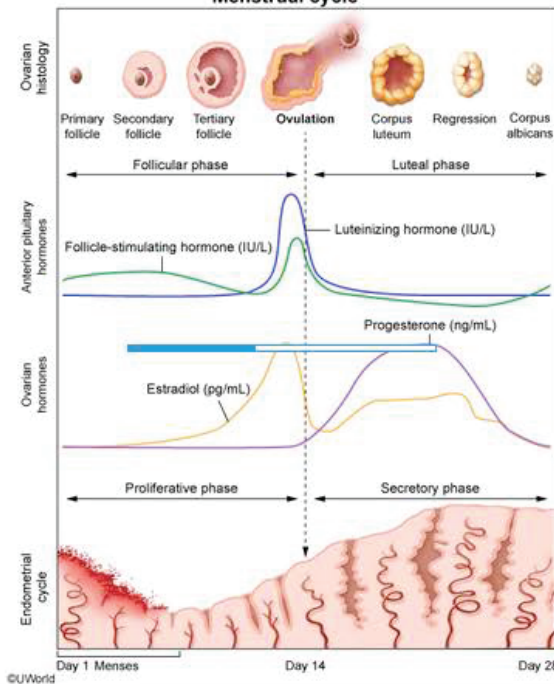
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## Menstrual cycle



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(Choice C) Endometrial hyperplasia is characterized by an increased endometrial gland to stroma ratio

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**(Choice C)** Endometrial hyperplasia is characterized by an increased endometrial gland to stroma ratio due to excess estrogen stimulation. Affected patients often present with irregular menses (eg, intermenstrual bleeding). In contrast, this patient has painful but regular menstrual cycles.

**(Choice D)** Multiple small follicular cysts in the ovaries and cortical fibrosis occur in polycystic ovary syndrome (PCOS). PCOS is associated with obesity, hirsutism, oligomenorrhea, and infertility. This patient's regular menses and absence of hyperandrogenism makes PCOS an unlikely etiology.

**(Choice E)** **Adenomyosis** is the presence of endometrial glands within the uterine myometrium. Abnormal uterine bleeding and painful menses are common, but the uterus is generally enlarged.

### Educational objective:

Endometriosis refers to the presence of endometrial glands and stroma outside the uterus. It may be asymptomatic or present with dysmenorrhea, dyspareunia, and/or infertility.

### References

- Practice Bulletin No. 114: Management of Endometriosis.
- Evaluation and Treatment of Endometriosis

Pathology Female Reproductive System & Breast Endometriosis

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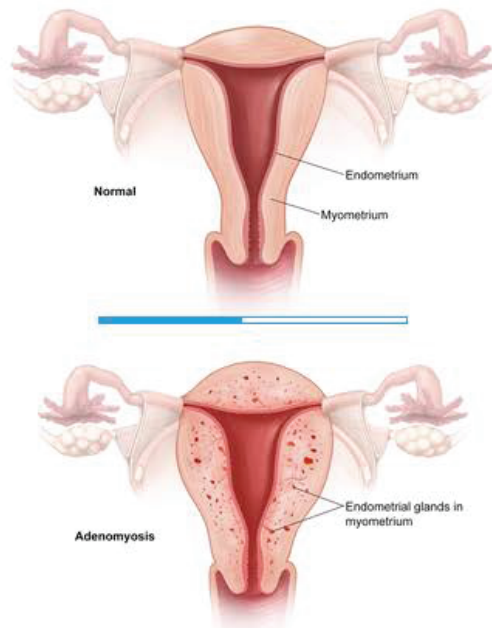
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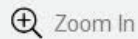
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## Exhibit Display

Normal uterus vs adenomyosis



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Settings

A 28-year-old woman comes to the office due to a 4-month history of amenorrhea. She has also had a whitish nipple discharge from both breasts. The patient has taken several pregnancy tests at home that have been negative. She has also had increased fatigue, depressed mood, and weight gain over this time. The patient has had no headaches or vision changes. She has no prior medical problems and takes no medications. On physical examination, there is thinning of the outer third of the eyebrows. The thyroid is enlarged and nontender to palpation. Abdominal and pelvic examinations are normal. The skin appears dry. Laboratory results are as follows:

Beta-hCG, serum	negative
Thyroxine (T4)	2.5 µg/dL
TSH	11.0 µU/mL
Prolactin	30 ng/mL (<20 ng/mL)
Antithyroid peroxidase antibodies	positive

Which of the following is the most likely mechanism causing this patient's elevated prolactin level?

☐ A. Activation of lactotrophs by antithyroid peroxidase antibodies



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Settings

Beta-hCG, serum

negative

Thyroxine (T4)

2.5 µg/dL

TSH

11.0 µU/mL

Prolactin

30 ng/mL (&lt;20 ng/mL)

Antithyroid peroxidase antibodies positive

Which of the following is the most likely mechanism causing this patient's elevated prolactin level?

- ☐ A. Activation of lactotrophs by antithyroid peroxidase antibodies
- ☐ B. Binding of dopamine receptors by antithyroid peroxidase antibodies
- ☐ C. Inhibition of dopamine release by TSH
- ☐ D. Stimulation of lactotrophs by thyrotropin-releasing hormone (TRH)
- ☐ E. TRH-induced overproduction of dopamine
- ☐ F. TSH-mediated activation of lactotrophs



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TSH

11.0  $\mu\text{U/mL}$

Prolactin

30 ng/mL (<20 ng/mL)

Antithyroid peroxidase antibodies positive

Which of the following is the most likely mechanism causing this patient's elevated prolactin level?

- ☐ A. Activation of lactotrophs by antithyroid peroxidase antibodies (3%)
- ☐ B. Binding of dopamine receptors by antithyroid peroxidase antibodies (5%)
- ☐ C. Inhibition of dopamine release by TSH (24%)
- ☒ D. Stimulation of lactotrophs by thyrotropin-releasing hormone (TRH) (49%)
- ☐ E. TRH-induced overproduction of dopamine (2%)
- ☐ F. TSH-mediated activation of lactotrophs (14%)

Correct

49%



02 mins, 30 secs



09/18/2020

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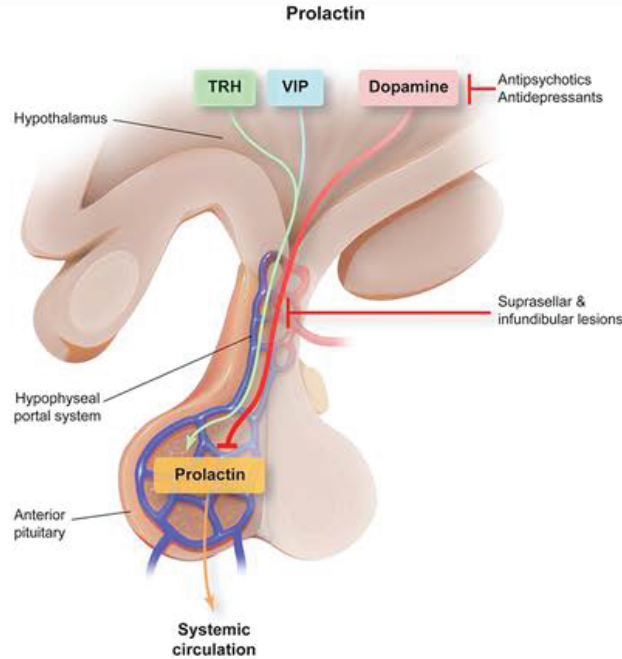
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### Exhibit Display



TRH = thyrotropin-releasing hormone; VIP = vasoactive intestinal peptide.

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TRH = thyrotropin-releasing hormone; VIP = vasoactive intestinal peptide.

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This patient has symptoms of hypothyroidism (eg, fatigue, weight gain, goiter, thinning of outer eyebrow edges). Her low thyroxine (T4), elevated TSH, and antithyroid peroxidase antibodies are further indicative of **primary hypothyroidism** from chronic autoimmune (Hashimoto) thyroiditis. In patients with primary hypothyroidism, there is a compensatory increase in hypothalamic thyrotropin-releasing hormone (TRH) production as thyroid hormone levels fall, stimulating increased secretion of TSH by the pituitary.

Prolactin is regulated primarily by the inhibitory effects of dopaminergic neurons from the hypothalamus. However, lactotroph cells express TRH receptors, and TRH stimulates synthesis and release of prolactin. The **elevated TRH levels** in the pituitary in patients with primary hypothyroidism can therefore **increase prolactin secretion** and lead to hyperprolactinemia.

In premenopausal women, hyperprolactinemia can cause **galactorrhea**. Prolactin suppresses GnRH secretion from the hypothalamus, leading to reduced secretion of LH (and to a lesser extent FSH) and subsequent hypogonadism, anovulation, and **amenorrhea**. Symptoms in men are often nonspecific, but can include infertility, decreased libido, and impotence.

**(Choices A and B)** The most common cause of primary hypothyroidism is chronic autoimmune (Hashimoto) thyroiditis. Most patients with Hashimoto thyroiditis produce thyroid peroxidase autoantibodies, but it is TRH (not the autoantibodies) that triggers prolactin release.





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**(Choices A and B)** The most common cause of primary hypothyroidism is chronic autoimmune (Hashimoto) thyroiditis. Most patients with Hashimoto thyroiditis produce thyroid peroxidase autoantibodies, but it is TRH (not the autoantibodies) that triggers prolactin release.

**(Choice C)** Antidopaminergic drugs (eg, antipsychotics, metoclopramide) can reduce the inhibitory effect of dopamine on prolactin secretion and lead to hyperprolactinemia, but TSH has little effect on dopamine pathways.

**(Choice E)** The stimulatory effect of TRH on pituitary lactotrophs is mediated by TRH receptors on lactotroph cells, not by effects on dopaminergic pathways. Overproduction of dopamine would inhibit lactotroph activity.

**(Choice F)** Effects of the hypothalamic-pituitary-thyroid axis on prolactin secretion are mediated primarily by TRH, not TSH.

### Educational objective:

Prolactin production is regulated primarily by inhibitory effects of hypothalamic dopaminergic pathways. However, prolactin secretion is stimulated by thyrotropin-releasing hormone (TRH). In patients with primary hypothyroidism, the increased production of TRH by the hypothalamus can lead to hyperprolactinemia.

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**(Choices A and B)** The most common cause of primary hypothyroidism is chronic autoimmune (Hashimoto) thyroiditis. Most patients with Hashimoto thyroiditis produce thyroid peroxidase autoantibodies, but it is TRH (not the autoantibodies) that triggers prolactin release.

**(Choice C)** Antidopaminergic drugs (eg, antipsychotics, metoclopramide) can reduce the inhibitory effect of dopamine on prolactin secretion and lead to hyperprolactinemia, but TSH has little effect on dopamine pathways.

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### Educational objective:

Prolactin production is regulated primarily by inhibitory effects of hypothalamic dopaminergic pathways. However, prolactin secretion is stimulated by thyrotropin-releasing hormone (TRH). In patients with primary hypothyroidism, the increased production of TRH by the hypothalamus can lead to hyperprolactinemia.

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Settings

A 33-year-old nulligravid woman comes to the office for evaluation of infertility. She has never been pregnant despite years of unprotected intercourse with her husband. She also has a history of pelvic pain, which worsens with menses. The pain has persisted despite medical therapy and is suspected to be due to endometriosis. Exploratory laparoscopy is performed, and multiple flesh-colored nodules are present on the pelvic organs, along with thin, filmy adhesions. In addition to having endometrial glands with hemosiderin pigment, one of the biopsies contains simple cuboidal epithelial cells. Which of the following is the most likely site of the biopsy?

- ☐ A. Cervix
- ☐ B. Endometrium
- ☐ C. Fallopian tube
- ☐ D. Ovary
- ☐ E. Peritoneum
- ☐ F. Vagina



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pregnant despite years of unprotected intercourse with her husband. She also has a history of pelvic pain, which worsens with menses. The pain has persisted despite medical therapy and is suspected to be due to **endometriosis**. Exploratory laparoscopy is performed, and multiple flesh-colored nodules are present on the pelvic organs, along with thin, filmy adhesions. In addition to having endometrial glands with hemosiderin pigment, one of the biopsies contains **simple cuboidal epithelial cells**. Which of the following is the most likely site of the biopsy?

- ☐ A. Cervix (12%)
- ☐ B. Endometrium (6%)
- ☐ C. Fallopian tube (14%)
- ☒ D. Ovary (58%)
- ☐ E. Peritoneum (5%)
- ☐ F. Vagina (2%)

Correct

58%

48 secs

12/01/2020

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### Epithelia of the female reproductive tract

Organ	Type	Key features
Ovary	Simple cuboidal (eg, germinal)	<ul style="list-style-type: none"> <li>Rapidly proliferate to repair ovulatory surface defects</li> </ul>
Fallopian tube	Simple columnar	<ul style="list-style-type: none"> <li>Ciliated cells transport egg/embryo</li> <li>Damage can cause infertility, hydrosalpinx, ectopic pregnancy</li> </ul>
Uterus	Simple columnar (eg, endometrium)	<ul style="list-style-type: none"> <li>Stratum functionalis sloughs off during menstruation</li> <li>Prolonged estrogen exposure prevents shedding, resulting in hyperplasia/malignancy</li> </ul>
Cervix	Ectocervix: stratified squamous non-keratinized  Endocervix: simple columnar	<ul style="list-style-type: none"> <li>Cervical glands secrete mucus:               <ul style="list-style-type: none"> <li>Thin and watery during ovulation</li> <li>Mucus plug in pregnancy</li> </ul> </li> <li>HPV infection predisposes to cervical malignancy</li> </ul>



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	columnar	malignancy
<b>Vagina</b>	Stratified squamous non-keratinized	<ul style="list-style-type: none"> <li>Maintains acidic environment to prevent infection</li> </ul>

HPV = human papillomavirus.

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The normal uterine mucosa (endometrium) is composed of simple columnar epithelium (**Choice B**), tubular glands, and stroma (connective tissue). **Endometriosis** is an important cause of chronic pain and infertility and is due to endometrial cells **implanted** on various pelvic organs, most commonly the ovary, posterior cul-de-sac, broad ligaments, and uterosacral ligaments. Histopathologic findings include **hemosiderin deposits** and **endometrial glands or stroma** outside of the uterus. As the endometrial implants shed through the menstrual cycle, they can accumulate old blood which appears as "**chocolate**"-colored fluid inside an ovarian cyst (endometrioma). Implants throughout the pelvis and abdomen can also appear as flesh-colored nodules, powder burn patterns, or adhesive disease.

The **ovary** is covered by **simple cuboidal cells** that divide and proliferate rapidly to repair ovarian surface defects from ovulation. Ectopic endometrial tissue may impair fertility by disrupting folliculogenesis, oocyte release, and oocyte fertilization.



release, and oocyte fertilization.

**(Choices A, C, and F)** Endometriosis involving the fallopian tubes is also common and can impair fertility by obstructing tubal transport. Implants on the cervix and vagina are rare.

**(Choice E)** The peritoneum has simple squamous epithelium (mesothelium) and is continuous with the cuboidal epithelium of the ovarian surface. These structures are frequent sites of endometriotic implants.

### Educational objective:

The uterine mucosa is covered by endometrium, and abnormal implantation of endometrial glands/stroma is referred to as endometriosis. The ovary is covered by a simple cuboidal epithelium involved in surface repair of defects from ovulation. Endometriosis commonly affects the ovary and results in infertility.

### References

- The developmental origin of cervical and vaginal epithelium and their clinical consequences: a systematic review.
- Human female reproductive tract epithelial cell culture.
- Endometriosis – Morphology, Clinical Presentations and Molecular Pathology



A 37-year-old woman comes to the emergency department due to sudden-onset nausea and severe right lower quadrant pain. The pain developed an hour ago after exercise and has become increasingly severe. The patient has no chronic medical conditions and has had no prior surgeries. She does not use contraception, and her last menstrual period was 3 weeks ago. Blood pressure is 136/94 mm Hg and pulse is 104/min. The abdomen is tender to palpation over the right lower quadrant. Pelvic ultrasound shows a right ovarian mass with no blood flow to the ovary. The specimen obtained from diagnostic laparoscopy and right oophorectomy is shown in the image below:



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Which of the following is the most likely diagnosis?

- ☐ A. Ectopic pregnancy
- ☐ B. Endometrioma
- ☐ C. Mature cystic teratoma
- ☐ D. Mucinous cystadenoma
- ☐ E. Ovarian fibroma
- ☐ F. Yolk sac tumor

**Submit**

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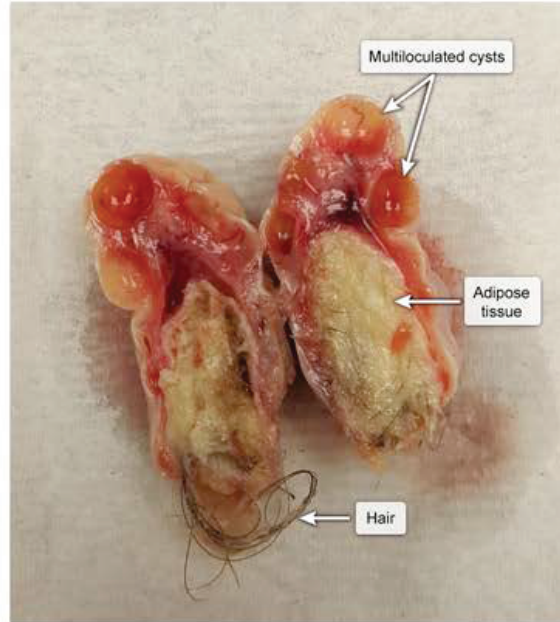


Which of the following is the most likely diagnosis?

- ☐ A. Ectopic pregnancy (0%)
- ☐ B. Endometrioma (0%)
- ☒ C. Mature cystic teratoma (96%)
- ☐ D. Mucinous cystadenoma (0%)
- ☐ E. Ovarian fibroma (0%)
- ☐ F. Yolk sac tumor (1%)

### Exhibit Display

Mature cystic teratoma



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This patient with sudden, severe right lower quadrant pain and absent blood flow to the ovary has ovarian torsion due to a **mature cystic teratoma** (ie, dermoid cyst). Dermoid cysts are benign germ cell tumors typically diagnosed in women age 10-30. Patients with a mature teratoma are often asymptomatic and diagnosed incidentally (eg, pelvic examination, ultrasound). However, the increase in ovarian bulk can **predispose to ovarian torsion** (rotation of the adnexa around the infundibulopelvic ligament); affected patients typically develop sudden, unilateral pelvic pain after physical activity (eg, exercise).

Teratomas have a gross appearance consistent with **all 3 germ cell layers** (ectoderm, mesoderm, endoderm). These pluripotent germ cells reside in the ovary and later differentiate into nonovarian tissue, including skin, hair, sebaceous glands (ectoderm); muscle, cartilage, fat (mesoderm); and thyroid or gastrointestinal tissue (endoderm). The typical teratoma is a **unilateral, multicystic** mass containing **yellow sebaceous fluid**, solid components (eg, teeth, cartilage), and **hair**.

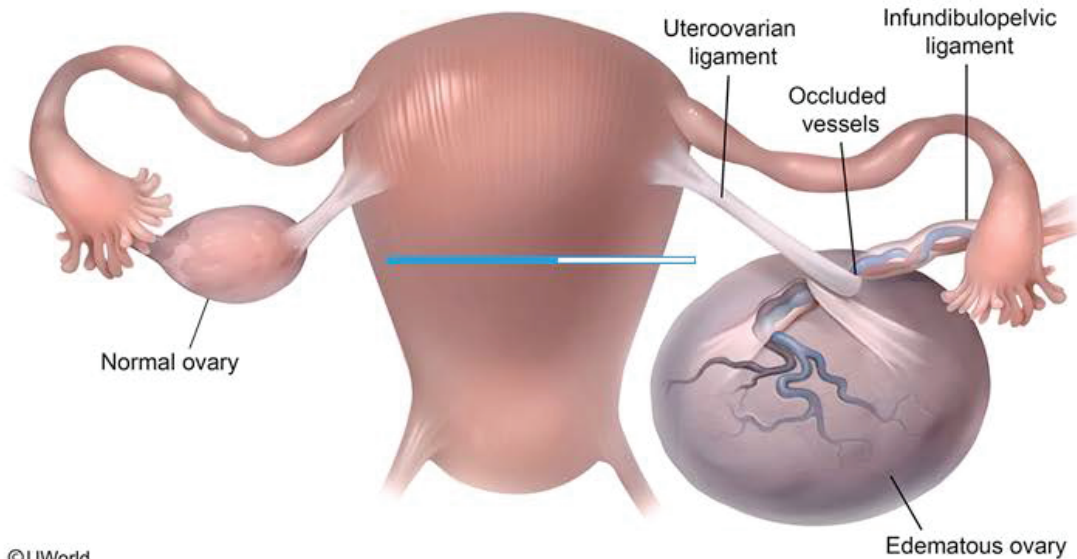
**(Choice A)** An **ectopic pregnancy** can implant on the ovary and cause nausea, abdominal pain, and an ovarian mass. However, gross pathology typically reveals products of conception (eg, embryo, chorionic villi).

**(Choice B)** **Endometriomas** are cystic masses of ectopic endometrial tissue and old blood that typically



Exhibit Display

Ovarian torsion



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(Choice B) Endometriomas are cystic masses of ectopic endometrial tissue and old blood that typically

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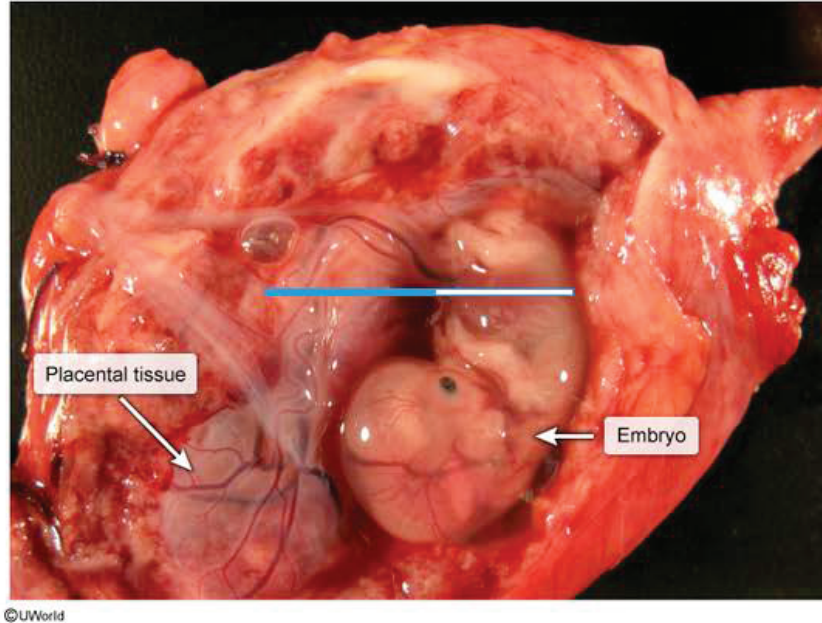
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Exhibit Display

Ectopic pregnancy



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(Choice B) Endometriomas are cystic masses of ectopic endometrial tissue and old blood that typically



ovarian mass. However, gross pathology typically reveals products of conception (eg, embryo, chorionic villi).

**(Choice B)** **Endometriomas** are cystic masses of ectopic endometrial tissue and old blood that typically have a homogenous, chocolate cyst appearance.

**(Choice D)** **Mucinous cystadenomas** are benign, surface epithelial ovarian masses that appear as thin-walled loculations of mucinous fluid; there is no associated hair.

**(Choice E)** **Ovarian fibromas** are sex cord tumors and have smooth capsules with homogeneously dense tissue composed of fibroblastic cells.

**(Choice F)** Yolk sac tumors are malignant germ cell tumors with gray-yellow, necrotic, and hemorrhagic areas on a gross specimen; there is no associated hair.

### Educational objective:

Mature cystic teratomas (ie, dermoid cysts) are derived from all 3 germ cell layers; therefore, the typical gross appearance is a multicystic mass containing yellow sebaceous fluid, solid components (eg, teeth, cartilage), and hair. Although often asymptomatic, affected patients are at increased risk of ovarian torsion.

### References

• [Bilateral dermoid ovarian torsion in a young woman: a case report](#)

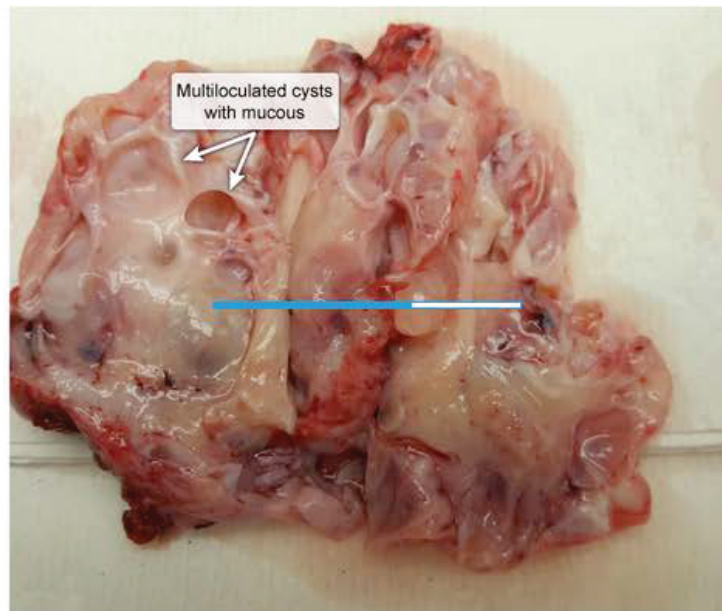




ovarian mass. However, gross pathology typically reveals products of conception (eg, embryo, chorionic

Exhibit Display

Mucinous cystadenoma



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Bilateral dermoid ovarian torsion in a young woman: a case report

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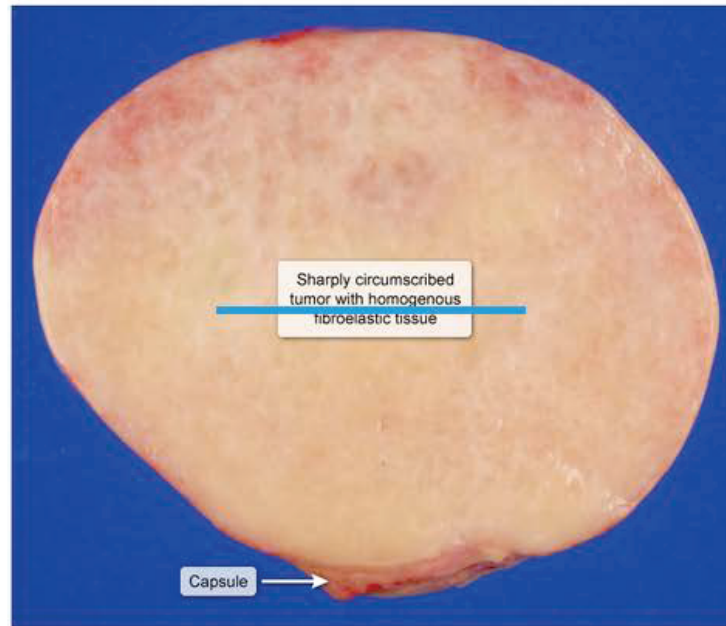
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ovarian mass. However, gross pathology typically reveals products of conception (eg, embryo, chorionic

### Exhibit Display

Ovarian fibroma



Sharply circumscribed tumor with homogenous fibroelastic tissue

Capsule

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A 25-year-old woman, gravida 4, para 0, comes to the office for evaluation of recurrent pregnancy loss. She has had 4 second-trimester losses with the same partner. The patient has menstrual cycles approximately 28 days with light bleeding for 2-3 days. Her past medical history is significant for left renal agenesis. Family history is negative for recurrent pregnancy loss. Laboratory studies are negative for anticardiolipin antibodies and lupus anticoagulant. Results of the patient's hysterosalpingogram are shown [exhibit](#). Based on her evaluation, a pelvic MRI is ordered and shows an abnormal contour to the uterine fundus. Failure of which of the following process is the most likely underlying mechanism of this patient's condition?

- ☐ A. Development of the paramesonephric ducts
- ☐ B. Fusion of the mesonephric ducts
- ☐ C. Involution of the paramesonephric ducts
- ☐ D. Lateral fusion of the paramesonephric ducts
- ☐ E. Vertical fusion with the urogenital sinus



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She has had 4 second-trimester losses with the same partner. The patient has menstrual cycles approximately 28 days with light bleeding for 2-3 days. Her past medical history is significant for left renal agenesis. Family history is negative for recurrent pregnancy loss. Laboratory studies are negative for anticardiolipin antibodies and lupus anticoagulant. Results of the patient's hysterosalpingogram are shown [exhibit](#). Based on her evaluation, a pelvic MRI is ordered and shows an abnormal contour to the uterine fundus. Failure of which of the following process is the most likely underlying mechanism of this patient's condition?

- ☐ A. Development of the paramesonephric ducts (9%)
- ☐ B. Fusion of the mesonephric ducts (18%)
- ☐ C. Involution of the paramesonephric ducts (10%)
- ☒ D. Lateral fusion of the paramesonephric ducts (56%)
- ☐ E. Vertical fusion with the urogenital sinus (5%)

Correct

56%  
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Time spent12/12/2020  
Last updated

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TUTOR

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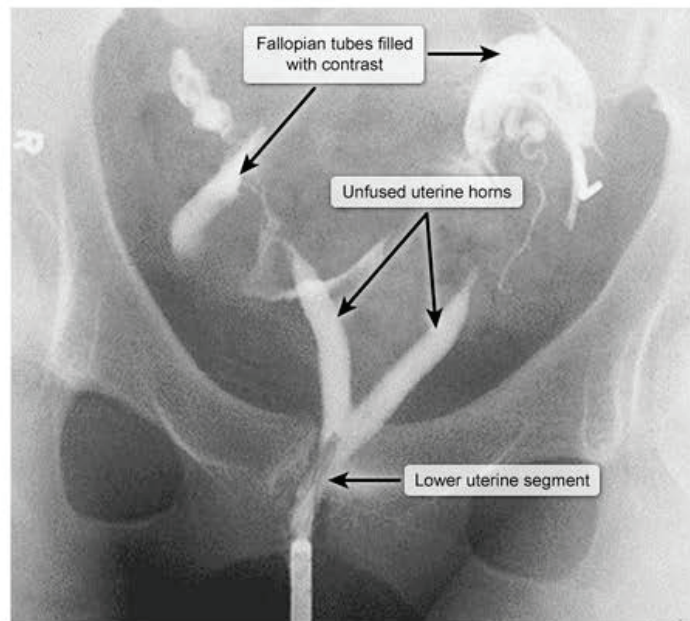
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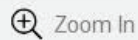
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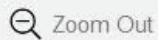
## Hysterosalpingogram of a lateral fusion defect



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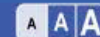


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Female reproductive tract development involves lateral/vertical fusion and involution of the **paramesonephric ducts (eg, müllerian ducts)**, which give rise to the fallopian tubes, uterus, cervix, and upper vagina. Development of the paramesonephric and **mesonephric ducts** is closely linked; therefore, uterine anomalies often coexist with **renal anomalies** (eg, unilateral renal agenesis).

**Failed lateral fusion** of the paramesonephric ducts can result in various anomalies. Incomplete lateral fusion of the upper segments can result in a **bicornuate** uterus characterized by an **indentation in the center of the fundus**. Complete lack of fusion can lead to uterine didelphys (double uterus and cervix). Failed involution of the paramesonephric ducts can result in a longitudinal uterine septum.

When a patient has difficulty conceiving or **recurrent pregnancy loss**, structural uterine anomalies can be screened by **hysterosalpingogram (HSG)**, which involves contrast injection through the cervix into the uterus with a concurrent pelvic x-ray. This patient's HSG shows 2 **unfused uterine horns** with a central filling defect, which can represent a bicornuate uterus or a longitudinal uterine septum (**Choice C**). **MRI** can distinguish these 2 anomalies as a septate uterus has a normal outer uterine contour.

**(Choice A)** Complete agenesis of the paramesonephric ducts leads to Mayer-Rokitansky-Küster-Hauser syndrome. The lower vagina originates from the urogenital sinus, and affected patients would experience





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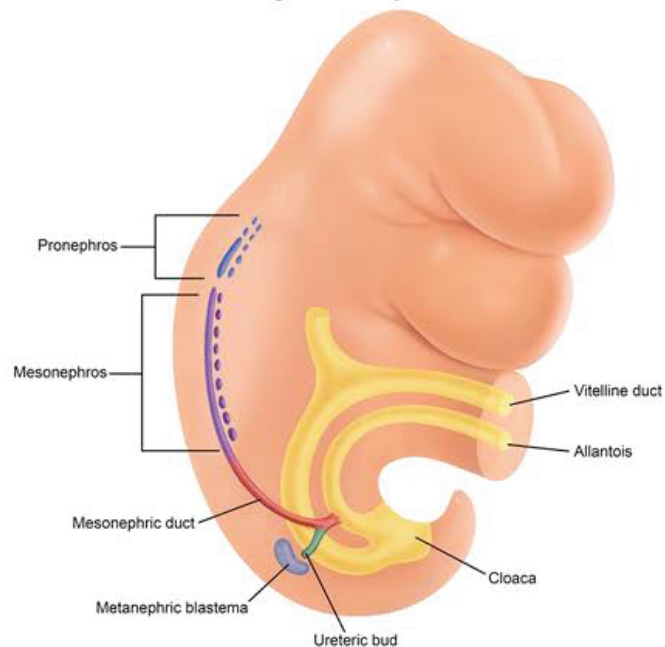
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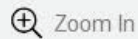
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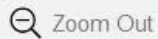
## Kidney development



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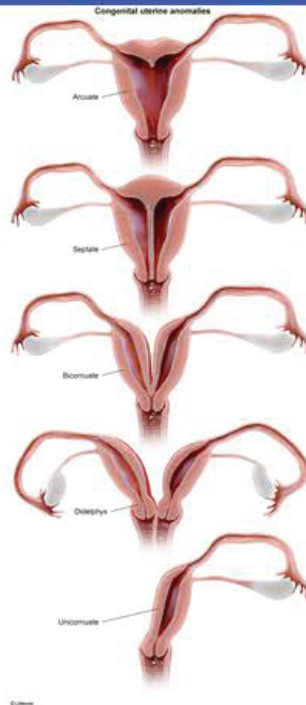


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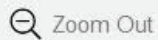


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## Exhibit Display



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When a patient has difficulty conceiving or **recurrent pregnancy loss**, structural uterine anomalies can be screened by **hysterosalpingogram (HSG)**, which involves contrast injection through the cervix into the uterus with a concurrent pelvic x-ray. This patient's HSG shows 2 **unfused uterine horns** with a central filling defect, which can represent a bicornuate uterus or a longitudinal uterine septum (**Choice C**). **MRI** can distinguish these 2 anomalies as a septate uterus has a normal outer uterine contour.

**(Choice A)** Complete agenesis of the paramesonephric ducts leads to Mayer-Rokitansky-Küster-Hauser syndrome. The lower vagina originates from the urogenital sinus, and affected patients would experience infertility due to a blind vaginal pouch and lack of müllerian structures.

**(Choice B)** The **mesonephric ducts** (eg, **wolffian ducts**) do not fuse during embryonic development. In females, the mesonephric ducts form Gartner ducts. In males, they form the epididymis, ductus deferens, seminal vesicles, and ejaculatory ducts.

**(Choice E)** A transverse vaginal septum is an example of failed vertical fusion of the paramesonephric ducts with the urogenital sinus. The obstructive septum causes primary amenorrhea with cyclic pelvic pain from hematometra (menses retained in the uterus), and an HSG cannot be performed on these patients.

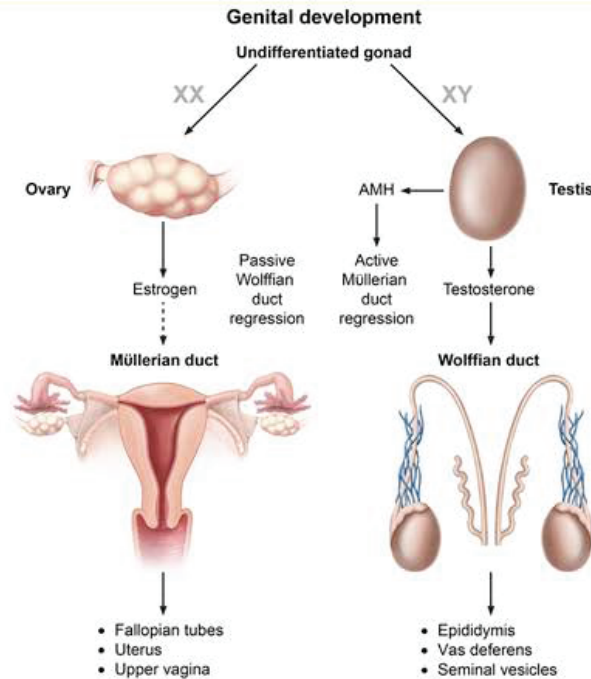
### Educational objective:

In females, the paramesonephric ducts fuse to form the fallopian tubes, uterus, cervix, and upper vagina.



When a patient has difficulty conceiving or recurrent pregnancy loss, structural uterine anomalies can be

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syndrome. The lower vagina originates from the urogenital sinus, and affected patients would experience infertility due to a blind vaginal pouch and lack of müllerian structures.

**(Choice B)** The [mesonephric ducts](#) (eg, [wolffian ducts](#)) do not fuse during embryonic development. In females, the mesonephric ducts form Gartner ducts. In males, they form the epididymis, ductus deferens, seminal vesicles, and ejaculatory ducts.

**(Choice E)** A transverse vaginal septum is an example of failed vertical fusion of the paramesonephric ducts with the urogenital sinus. The obstructive septum causes primary amenorrhea with cyclic pelvic pain from hematometra (menses retained in the uterus), and an HSG cannot be performed on these patients.

### Educational objective:

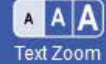
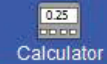
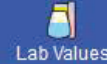
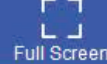
In females, the paramesonephric ducts fuse to form the fallopian tubes, uterus, cervix, and upper vagina. Disruptions of this process can lead to a variety of müllerian tract anomalies, and renal anomalies are a common comorbidity. Incomplete lateral fusion of the paramesonephric ducts results in a bicornuate uterus characterized by an indentation in the center of the fundus.

### References

- [Müllerian duct anomalies: Embryological development, classification, and MRI assessment.](#)
- [Unilateral renal agenesis and female genital tract pathologies.](#)







A 24-year-old woman, gravida 1 para 1, comes to the office for an annual visit. The patient is up to date with cervical cancer screening and has completed the human papillomavirus vaccination series. She is in a monogamous relationship with her husband and has negative chlamydia and gonorrhea screening. The patient has been using a progestin-only pill since giving birth a year ago. She would like to switch to a combined oral contraceptive as she is no longer breastfeeding. Which of the following will be the primary mechanism of pregnancy prevention when the patient switches to a combined hormonal oral contraceptive?

- ☐ A. Impairment of embryo implantation
- ☐ B. Impairment of sperm penetration into the uterus
- ☐ C. Increase in gonadotropin-releasing hormone activity
- ☐ D. Intrauterine environment toxic to sperm
- ☐ E. Reduction of serum gonadotropin levels
- ☐ F. Reduction of serum prolactin level





with cervical cancer screening and has completed the human papillomavirus vaccination series. She is in a monogamous relationship with her husband and has negative chlamydia and gonorrhea screening. The patient has been using a progestin-only pill since giving birth a year ago. She would like to switch to a combined oral contraceptive as she is no longer breastfeeding. Which of the following will be the primary mechanism of pregnancy prevention when the patient switches to a combined hormonal oral contraceptive?

- ☐ A. Impairment of embryo implantation (12%)
- ☐ B. Impairment of sperm penetration into the uterus (6%)
- ☐ C. Increase in gonadotropin-releasing hormone activity (5%)
- ☐ D. Intrauterine environment toxic to sperm (1%)
- ☒ E. Reduction of serum gonadotropin levels (73%)
- ☐ F. Reduction of serum prolactin level (0%)

Correct

73%  
Answered correctly01 min, 05 secs  
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## Contraceptives

Methods	Primary mechanism of action
<b>Systemic progestins</b> <ul style="list-style-type: none"><li>• Combined hormonal contraceptive (pill, transdermal patch, vaginal ring)</li><li>• Progestin implant/injection</li></ul>	Suppresses GnRH & pituitary gonadotropin secretion, inhibiting ovulation
<b>Locally-acting progestins</b> <ul style="list-style-type: none"><li>• Progestin-only (norethindrone) pill</li><li>• Levonorgestrel IUD</li></ul>	Thickens cervical mucus, impairing sperm penetration
<ul style="list-style-type: none"><li>• Copper IUD</li></ul>	Creates chronic cytotoxic inflammatory response in uterus, impairing sperm migration

Combined = the combination of ethinyl estradiol & a progestin;  
GnRH = gonadotropin-releasing hormone; IUD = intrauterine device.

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**Progestin**, the synthetic equivalent to progesterone, is responsible for pregnancy prevention in all hormonal contraceptives. Estrogen is often included to improve the bleeding profile.

The primary mechanism of action of a progestin depends on its pharmacokinetics (type of progestin, mode of administration, dose). Progestins that are more potent produce both **systemic** and local effects (levonorgestrel in pill form), whereas less potent progestins produce **local** uterine effects only (levonorgestrel released by the intrauterine device). **Combined hormonal contraceptives** exhibit systemic effects by **suppressing GnRH in the hypothalamus**, which decreases synthesis of the gonadotropins FSH and LH in the anterior pituitary. Because an LH spike is required to stimulate **ovulation**, **ovulation is inhibited**.

**(Choice A)** All progestin-containing contraceptives thin the uterine lining, which may theoretically impair embryo implantation. However, combined hormonal contraceptives prevent ovulation from occurring, thereby preventing the opportunity for fertilization in the first place and making this mechanism in pregnancy prevention unlikely.

**(Choice B)** The progestin-only pill (due to low dosage/potency) and **levonorgestrel intrauterine device** (IUD) prevent pregnancy by thickening cervical mucus, which prevents sperm from accessing the uterus. It





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(IUD) prevent pregnancy by thickening cervical mucus, which prevents sperm from accessing the uterus. It lacks the systemic effects of combined hormonal contraceptives, and women continue to have ovulatory cycles.

**(Choice C)** The fertility drug clomiphene citrate is a selective estrogen receptor modulator that stimulates FSH and LH production, which in turn stimulates follicular development in the ovaries. Clomiphene citrate has the opposite effect of systemically acting progestins and increases the chance of pregnancy.

**(Choice D)** The **copper IUD** releases copper ions that elicit an inflammatory reaction in the uterus that is toxic to sperm and prevents fertilization.

**(Choice F)** Dopamine agonists (eg, bromocriptine, cabergoline) are used to treat hyperprolactinemia by decreasing prolactin secretion by binding dopamine receptors. Contraceptives do not have a direct effect on prolactin.

### Educational objective:

All hormone-containing contraceptives prevent pregnancy through the actions of progestins. The main mechanism of contraceptives with systemically active progestins (eg, combined hormonal oral contraceptives) is inhibiting ovulation by decreasing FSH and LH synthesis in the anterior pituitary.

### References





A 38-year-old woman comes to the office for follow up of symptomatic uterine fibroids. The patient has a history of heavy menstrual bleeding, with monthly cycles lasting 7-10 days and brisk blood flow with the passage of large clots. Four months ago, the patient went to the emergency department due to an acute episode of heavy menstrual bleeding. Pelvic examination revealed an enlarged fibroid uterus, and she was found to have significant blood loss anemia. The patient was prescribed continuous leuprolide therapy at that time. This medication has most likely had which of the following effects on this patient's hormone levels?

	GnRH	FSH	Estrogen
<input type="radio"/> A.	↑	↑	↑
<input type="radio"/> B.	↑	↑	↓
<input type="radio"/> C.	↑	↓	↓
<input type="radio"/> D.	↓	↓	↑
<input type="radio"/> E.	↓	↓	↓







history of heavy menstrual bleeding, with monthly cycles lasting 7-10 days and brisk blood flow with the passage of large clots. Four months ago, the patient went to the emergency department due to an acute episode of heavy menstrual bleeding. Pelvic examination revealed an enlarged fibroid uterus, and she was found to have significant blood loss anemia. The patient was prescribed continuous leuprolide therapy at that time. This medication has most likely had which of the following effects on this patient's hormone levels?

	GnRH	FSH	Estrogen	
<input type="radio"/> A.	↑	↑	↑	(0%)
<input type="radio"/> B.	↑	↑	↓	(0%)
<input type="radio"/> C.	↑	↓	↓	(0%)
<input type="radio"/> D.	↓	↓	↑	(0%)
<input checked="" type="radio"/> E.	↓	↓	↓	(100%)

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02/23/2021

Last Updated

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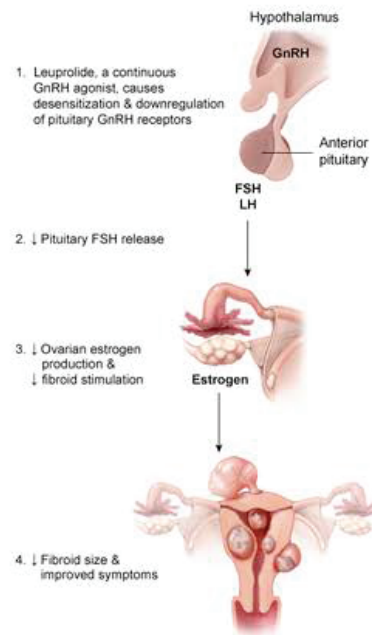
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## Exhibit Display

## Leuprolide treatment of uterine fibroids



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This patient has symptomatic uterine fibroids (ie, leiomyomas), benign, estrogen-dependent tumors that can cause bulk (eg, pelvic pressure, constipation) or bleeding symptoms such as heavy menses and blood loss anemia.

Patients with symptomatic fibroids may be treated with **leuprolide**, a **GnRH receptor agonist** that inhibits endogenous hypothalamic GnRH release and initially stimulates gonadotropin (ie, FSH, LH) secretion from the pituitary. However, unlike endogenous GnRH, which is released in a pulsatile fashion, **continuous leuprolide therapy** (eg, depot injection formulations) eventually causes desensitization and downregulation of pituitary GnRH receptors, leading to **decreased FSH** (hypogonadotropic) and **decreased estrogen** (hypogonadal) levels.

This hypogonadotropic, hypogonadal state can **shrink estrogen-dependent fibroids** and induce amenorrhea, thereby improving bleeding symptoms. However, patients typically also experience intolerable menopausal symptoms (eg, vasomotor symptoms, decreased bone density); therefore, leuprolide is typically used short term (eg, 3-6 months) to decrease fibroid size and to improve anemia prior to surgical management.

**(Choice A)** Clomiphene, used for ovulation induction to treat infertility, acts on the hypothalamus by





leuprolide is typically used short-term (eg, 3–6 months) to decrease tumor size and to improve anemia prior to surgical management.

**(Choice A)** Clomiphene, used for ovulation induction to treat infertility, acts on the hypothalamus by interfering with hypothalamic estrogen receptors, thereby inhibiting normal negative feedback from estrogen; this promotes GnRH and FSH secretion and stimulates ovulation.

**(Choice B)** Letrozole, an aromatase inhibitor, decreases peripheral (ie, adipose) and ovarian conversion of androgens to estrogens; the decreased estrogen level releases estrogenic negative feedback on the hypothalamus to increase GnRH and FSH secretion. Letrozole is used as adjuvant therapy for estrogen receptor–positive breast cancer in postmenopausal women (by decreasing estrogen levels) and for ovulation induction (by stimulating GnRH and FSH release).

**(Choice C)** Depot medroxyprogesterone acetate (DMPA), a progesterone contraceptive, inhibits pituitary secretion of gonadotropins (ie, FSH, LH) to prevent ovulation. The decrease in FSH causes increased hypothalamic GnRH secretion and suppressed ovarian estrogen production.

**(Choice D)** Exogenous estrogen–containing medications (eg, combined estrogen-progestin oral contraceptives, menopausal hormone therapy) increase estrogen levels, producing negative feedback at the hypothalamus and decreased GnRH and FSH levels.



androgens to estrogens; the decreased estrogen level releases estrogenic negative feedback on the hypothalamus to increase GnRH and FSH secretion. Letrozole is used as adjuvant therapy for estrogen receptor–positive breast cancer in postmenopausal women (by decreasing estrogen levels) and for ovulation induction (by stimulating GnRH and FSH release).

**(Choice C)** Depot medroxyprogesterone acetate (DMPA), a progesterone contraceptive, inhibits pituitary secretion of gonadotropins (ie, FSH, LH) to prevent ovulation. The decrease in FSH causes increased hypothalamic GnRH secretion and suppressed ovarian estrogen production.

**(Choice D)** Exogenous estrogen–containing medications (eg, combined estrogen-progestin oral contraceptives, menopausal hormone therapy) increase estrogen levels, producing negative feedback at the hypothalamus and decreased GnRH and FSH levels.

### Educational objective:

Leuprolide is a GnRH agonist used to treat symptomatic uterine fibroids (eg, heavy menses, anemia). When administered in a continuous fashion, leuprolide inhibits the release of endogenous hypothalamic GnRH and downregulates pituitary GnRH receptors, thereby decreasing GnRH, FSH, and estrogen levels (ie, hypogonadotropic hypogonadism).

### References





A 22-year-old woman, who recently relocated, comes to the office for a new patient visit. She has mild intellectual disability and has completed a high school level of education. The patient has no major health problems but reports persistent swelling of the hands and feet. Menarche occurred at age 13, and she has regular menstrual cycles. Physical examination shows short stature and a webbed neck. Karyotype analysis performed on peripheral leukocytes shows that 40% of the cells have a 45,X genotype and that the remaining 60% contain a 46,XX genotype. Which of the following is the most likely cause of this patient's condition?

- ☐ A. Chromosomal deletion
- ☐ B. Complete monosomy X
- ☐ C. Germline mosaicism
- ☐ D. Somatic mosaicism
- ☐ E. Uniparental disomy
- ☐ F. X chromosome inactivation







intellectual disability and has completed a high school level of education. The patient has no major health problems but reports persistent swelling of the hands and feet. Menarche occurred at age 13, and she has regular menstrual cycles. Physical examination shows short stature and a webbed neck. Karyotype analysis performed on peripheral leukocytes shows that 40% of the cells have a 45,X genotype and that the remaining 60% contain a 46,XX genotype. Which of the following is the most likely cause of this patient's condition?

- ☐ A. Chromosomal deletion (1%)
- ☐ B. Complete monosomy X (2%)
- ☐ C. Germline mosaicism (34%)
- ☒ D. Somatic mosaicism (53%)
- ☐ E. Uniparental disomy (2%)
- ☐ F. X chromosome inactivation (5%)

Correct



53%

Answered correctly



53 secs

Time spent



10/21/2020

Last updated

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Item 4 of 40

Question Id: 12225



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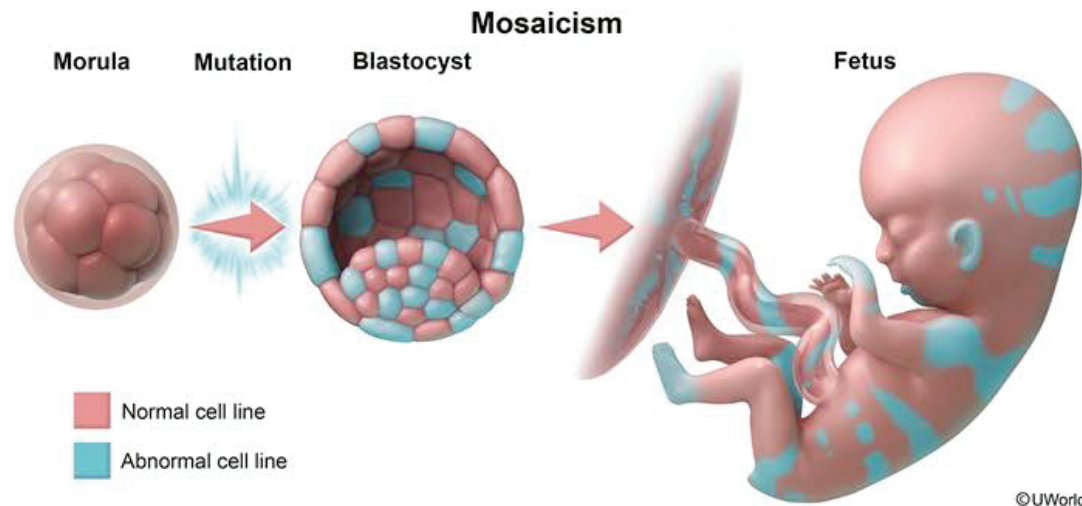


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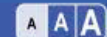
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This patient with mild intellectual disability, lymphedema, short stature, webbed neck, and 2 karyotypes evident on analysis likely has **mosaic Turner syndrome**. Mosaicism is defined as the presence of multiple, **genetically different cell lines** within the body. It can result from several processes, including chromosomal nondisjunction and mutations during the first stages of embryonic development. The earlier the error happens, the more daughter cells are affected.

**Mosaicism** can be classified as germline, somatic, or both:

- **Somatic mosaicism** affects the cells forming the body, causing **disease manifestations** to develop in affected individuals. 45,X/46,XX is the most commonly diagnosed mosaicism affecting sex chromosomes. These patients typically have a milder form of Turner syndrome or can be asymptomatic, depending on the ratio of abnormal to normal cells.
- **Germline mosaicism** affects the cells that give rise to gametes, allowing the affected genes to **pass to the offspring**. The chance of a child being affected depends on the proportion of gametes that carry the mutation. When mosaicism is limited to the germline, the affected parent does not develop clinical manifestations.

**(Choice A)** Chromosomal deletions can be either macro or micro, depending on how many base pairs are

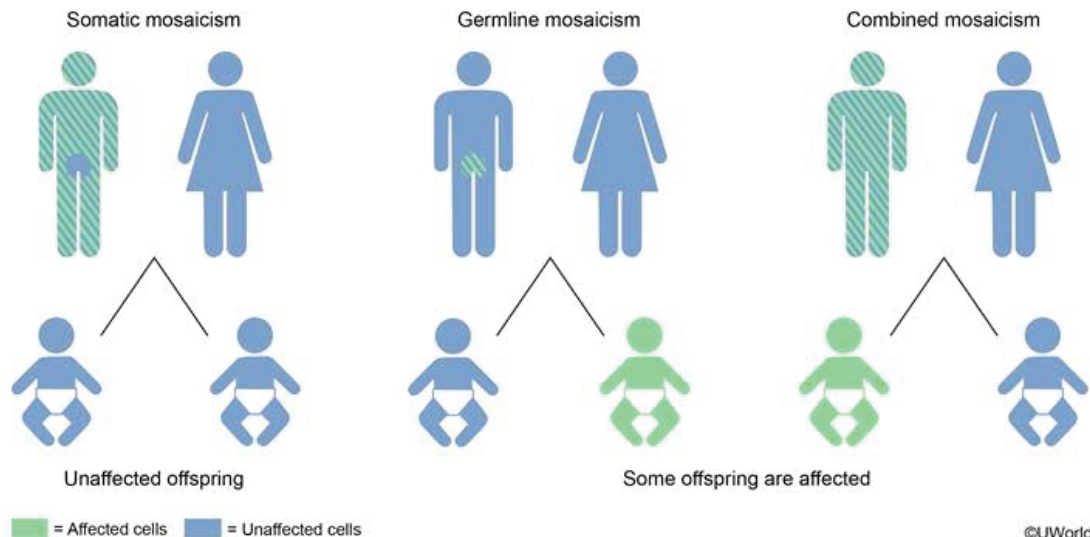




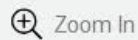


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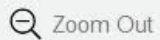
## Mosaicism



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clinical manifestations.

**(Choice A)** Chromosomal deletions can be either macro or micro, depending on how many base pairs are eliminated. Neither process results in the elimination of entire chromosomes or the presence of multiple cell lines within the body.

**(Choice B)** Complete monosomy X also causes Turner syndrome. However, it would not explain the 2 separate genotypes seen on karyotyping.

**(Choice C)** This patient has manifestations of Turner syndrome and peripheral cells with multiple distinct genotypes, which indicates that she has somatic mosaicism. If the mitotic error occurred very early in embryogenesis, before separation of the germline, she could also have germline mosaicism. However, germline mosaicism would not be the cause of her clinical manifestations and would not be detectable on karyotyping of a blood sample.

**(Choice E)** Uniparental disomy describes the phenomenon wherein both chromosomes in a given pair come from one parent. In such cases, patients still have the full complement of chromosomes on karyotyping.

**(Choice F)** In women, one X chromosome is normally inactivated in each somatic cell to maintain proper





germline mosaicism would not be the cause of her clinical manifestations and would not be detectable on karyotyping of a blood sample.

**(Choice E)** Uniparental disomy describes the phenomenon wherein both chromosomes in a given pair come from one parent. In such cases, patients still have the full complement of chromosomes on karyotyping.

**(Choice F)** In women, one X chromosome is normally inactivated in each somatic cell to maintain proper gene dosage. Despite the presence of only one functional X chromosome in each cell, both are still detectable on karyotyping.

### Educational objective:

Mosaicism is defined as the presence of multiple, genetically different cell lines within the body. It can result from several processes, including chromosomal nondisjunction or a mutation during the first stages of embryonic development. Somatic mosaicism results in a mixture of normal and mutated somatic cells, often leading to a milder form of the disease.

### References

- [Turner syndrome: diagnosis and management.](#)
- [Genetic considerations in the patient with Turner syndrome--45,X with or without mosaicism.](#)







A 28-year-old woman comes to the office for a preconception visit. She has never been pregnant and would like to know how to improve her chances of conceiving. The patient has no family history of genetic abnormalities or infertility. Menarche was at age 13. She menstruates every 28 days, and bleeding lasts for 4 days. She has had no prior surgeries or sexually transmitted infections. Her husband has not fathered a child and has no urogenital problems. The couple has intercourse several times a month. Which of the following hormones would increase the most in concentration after ovulation?

- ☐ A. Androstenedione
- ☐ B. Estrogen
- ☐ C. FSH
- ☐ D. GnRH
- ☐ E. LH
- ☐ F. Progesterone

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A 28-year-old woman comes to the office for a preconception visit. She has never been pregnant and would like to know how to improve her chances of conceiving. The patient has no family history of genetic abnormalities or infertility. Menarche was at age 13. She menstruates every 28 days, and bleeding lasts for 4 days. She has had no prior surgeries or sexually transmitted infections. Her husband has not fathered a child and has no urogenital problems. The couple has intercourse several times a month. Which of the following hormones would increase the most in concentration after ovulation?

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- ☐ C. FSH
- ☐ D. GnRH
- ☐ E. LH
- ☐ F. Progesterone

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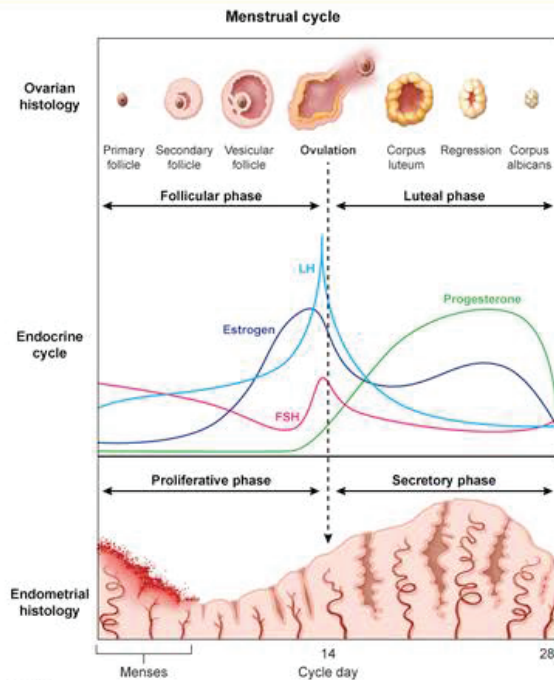
- ☐ A. Androstenedione (0%)
- ☐ B. Estrogen (2%)
- ☐ C. FSH (1%)
- ☐ D. GnRH (0%)
- ☐ E. LH (5%)
- ☒ F. Progesterone (90%)







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The primary hormones involved in the menstrual cycle are FSH and LH (both from the anterior pituitary) and progesterone and estrogen (both from the ovaries). Many of these names signify their function (eg, progesterone = progestation).

Following the onset of menstruation (day 1), pituitary FSH stimulates the ovary to recruit 1 primary follicle, which becomes the **dominant follicle**. FSH stimulates granulosa cells inside the follicle to produce estrogen, leading to a **progressive rise in serum estrogen**. During the 14-day maturation process (follicular phase of the menstrual cycle), the follicle enlarges and becomes fluid-filled, and the primary oocyte becomes a secondary oocyte (**tertiary or mature follicle**). Peak levels of estrogen (**Choice B**) in the late follicular phase have a positive feedback effect on LH production, causing an "**LH surge**" (**Choice E**). Ultimately, this LH surge causes the rupture of the follicle, leading to extrusion of the secondary oocyte (**ovulation**). FSH levels are also highest just before ovulation (**Choice C**). Both LH and FSH surges are mediated through changes in the level and pulsatility of **GnRH (Choice D)**, which is also highest before ovulation.

**Following ovulation**, the granulosa and theca cells of the ovarian follicle luteinize to form the **corpus luteum**; this secretes relatively **high levels of progesterone** and moderate levels of estrogen for the next 14 days (the luteal phase of the menstrual cycle). Progesterone stimulates the endometrium to transform from proliferative to **secretory** to become a hospitable environment for implantation.





ovulation.

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**(Choice A)** Androstenedione is a weak androgen and a precursor to testosterone and estrogen, not progesterone. In women, androstenedione is synthesized from cholesterol in ovarian theca cells and aromatized to estrogen in granulosa cells. Peak serum levels would occur before ovulation.

### Education objective:

Of all hormones influencing the menstrual cycle (LH, FSH, estrogen, progesterone), progesterone increases the most in concentration after ovulation. During the latter half of the menstrual cycle, the corpus luteum secretes high levels of progesterone, which thickens the endometrium and prepares it to receive and nourish a blastocyst.

### References

- [The endocrinology of the menstrual cycle.](#)







A 34-year-old nulligravid woman comes to the office due to vulvar itching and vaginal discharge. She has no other concerns. The patient is sexually active with her fiancé and takes oral contraceptives daily. She does not use barrier contraception. She took antibiotics 2 weeks ago for sinusitis but has no other medical problems. Pelvic examination shows an erythematous vulva and a thick white discharge that adheres to the vaginal wall. The rest of the physical examination is normal. Microscopic examination reveals budding cells. Which of the following is the most likely underlying cause of her current condition?

- ☐ A. Decreased glycogen concentration in the vaginal epithelium
- ☐ B. Decreased number of gram-positive bacteria in the vagina
- ☐ C. Decreased thickness of the vaginal epithelium
- ☐ D. Increased alkaline secretions by the cervical mucosa
- ☐ E. Viral DNA incorporation into lower genital epithelia

**Submit**



A 34-year-old nulligravid woman comes to the office due to vulvar itching and vaginal discharge. She has no other concerns. The patient is sexually active with her fiancé and takes oral contraceptives daily. She does not use barrier contraception. She took antibiotics 2 weeks ago for sinusitis but has no other medical problems. Pelvic examination shows an erythematous vulva and a thick white discharge that adheres to the vaginal wall. The rest of the physical examination is normal. Microscopic examination reveals budding cells. Which of the following is the most likely underlying cause of her current condition?

- ☐ A. Decreased glycogen concentration in the vaginal epithelium (6%)
- ☒ B. Decreased number of gram-positive bacteria in the vagina (70%)
- ☐ C. Decreased thickness of the vaginal epithelium (2%)
- ☐ D. Increased alkaline secretions by the cervical mucosa (19%)
- ☐ E. Viral DNA incorporation into lower genital epithelia (1%)

Correct



70%

Answered correctly



01 min, 15 secs

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11/08/2020

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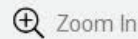


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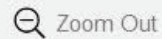
## Differential diagnosis of vaginitis

Bacterial vaginosis ( <i>Gardnerella vaginalis</i> )	Trichomoniasis ( <i>Trichomonas vaginalis</i> )	Candida vaginitis ( <i>Candida albicans</i> )
		
<ul style="list-style-type: none"><li>• Thin, off-white discharge with fishy odor</li><li>• No inflammation</li></ul>	<ul style="list-style-type: none"><li>• Thin, yellow-green, malodorous, frothy discharge</li><li>• Vaginal inflammation</li></ul>	<ul style="list-style-type: none"><li>• Thick, "cottage cheese" discharge</li><li>• Vaginal inflammation</li></ul>
		
<ul style="list-style-type: none"><li>• pH &gt;4.5</li><li>• Clue cells</li><li>• Positive whiff test (amine odor with KOH)</li></ul>	<ul style="list-style-type: none"><li>• pH &gt;4.5</li><li>• Motile trichomonads</li></ul>	<ul style="list-style-type: none"><li>• Normal pH (3.8 - 4.5)</li><li>• Pseudohyphae</li></ul>
Metronidazole or clindamycin	Metronidazole; treat sexual partner	Fluconazole

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Gram-positive lactobacilli comprise a major part of the normal vaginal flora and exist in balance with other colonizers at a normal vaginal pH of 3.8-4.5. Changes in vaginal flora and epithelial injury can lead to overgrowth of yeast, most commonly *Candida*. Common triggers for ***Candida* vaginitis** include the following:

- **Antibiotic use**
- **High estrogen** levels (eg, pregnancy)
- Systemic **corticosteroid therapy**
- Uncontrolled **diabetes mellitus**
- Any other cause of **immunosuppression**, including HIV

Antibiotic use is the most common cause of *Candida* vaginitis due to **reduction of the lactobacilli population**, which facilitates *Candida* overgrowth. Patients with *Candida* vaginitis have vulvar/vaginal pruritus and erythema and a thick, white "cottage cheese-like" discharge. Vaginal pH is typically unchanged. Wet mount examination with potassium hydroxide (KOH) preparation is diagnostic and reveals budding yeast and pseudohyphae.

**(Choices A and C)** Decreased thickness of the vaginal epithelium and decreased amounts of glycogen in epithelial cells are characteristic in postmenopausal and lactating women. These changes are caused by



budding yeast and pseudohyphae.

**(Choices A and C)** Decreased thickness of the vaginal epithelium and decreased amounts of glycogen in epithelial cells are characteristic in postmenopausal and lactating women. These changes are caused by low estrogen levels and lead to atrophic vaginitis.

**(Choice D)** Elevated pH of vaginal secretions ( $>4.5$ ) is associated with bacterial vaginosis and *Trichomonas* vaginitis, not *Candida* vaginitis.

**(Choice E)** Human papillomavirus (HPV) has a predilection for anogenital keratinized skin and mucous membranes. HPV can cause warts, dysplasia, and malignancy by incorporating its DNA into anogenital epithelial cells.

### Educational objective:

Antibiotics suppress the normal vaginal flora and facilitate *Candida* overgrowth. Antibiotic use is the most common cause of *Candida* vaginitis. Other potential causes include pregnancy, systemic corticosteroid use, diabetes mellitus, and immunosuppression.

### References

- ACOG Practice Bulletin. Clinical management guidelines for obstetrician-gynecologists, Number 72, May 2006: Vaginitis.



A 15-year-old girl is brought to the physician for evaluation of primary amenorrhea. Her mother is concerned because her other daughters had menarche before age 13. Vital signs are normal. The patient is at the 5th percentile for height and 20th percentile for weight. Examination shows a high arched palate and Tanner stage I breasts with inverted and widely spaced nipples. Further evaluation would most likely show which of the following?

- ☐ A. Absent uterus
- ☐ B. Ambiguous genitalia
- ☐ C. Atrophic ovaries
- ☐ D. Fibrosed fallopian tubes
- ☐ E. Hirsutism
- ☐ F. Vaginal agenesis

**Submit**





A 15-year-old girl is brought to the physician for evaluation of primary amenorrhea. Her mother is concerned because her other daughters had menarche before age 13. Vital signs are normal. The patient is at the 5th percentile for height and 20th percentile for weight. Examination shows a high arched palate and Tanner stage I breasts with inverted and widely spaced nipples. Further evaluation would most likely show which of the following?

- ☐ A. Absent uterus (5%)
- ☐ B. Ambiguous genitalia (4%)
- ☒ C. Atrophic ovaries (83%)
- ☐ D. Fibrosed fallopian tubes (2%)
- ☐ E. Hirsutism (2%)
- ☐ F. Vaginal agenesis (2%)

Correct



83%

Answered correctly



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01/21/2021

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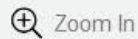
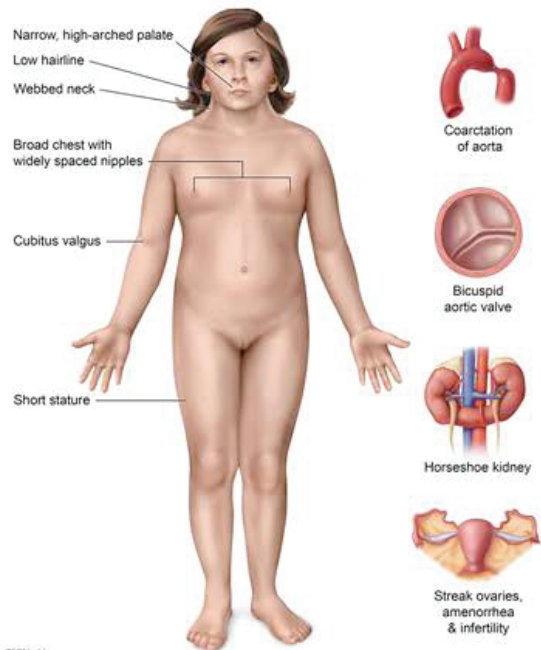
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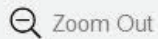
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## Turner syndrome



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**Primary amenorrhea** is defined as the absence of menses by age 15 in someone who has normal growth and secondary sexual characteristics (eg, body hair growth, breast development) or absence of menses by age 13 in girls without secondary sex characteristics. Chromosomal abnormalities resulting in ovarian insufficiency are the most common cause of primary amenorrhea.

This patient's short stature, high arched palate, Tanner I breasts, and widely spaced nipples are characteristic of **Turner syndrome (45,XO)**. Patients with Turner syndrome have a variable degree of **ovarian dysgenesis**. The ovaries usually appear underdeveloped and atrophic ("streak gonads") due to in utero degeneration of the ovarian follicles with replacement by fibrotic tissue. Since menstruation and breast development are estrogen-dependent processes, they do not occur because the ovaries are nonfunctional.

**(Choice A)** Although patients with Turner syndrome may have streak ovaries, the uterus should be present. An absent uterus and primary amenorrhea can be seen in Müllerian agenesis and androgen insensitivity syndrome.

**(Choice B)** Turner syndrome patients have normal female external genitalia. Ambiguous external genitalia can be seen in 46,XX patients with congenital adrenal hyperplasia.





**(Choice A)** Although patients with Turner syndrome may have streak ovaries, the uterus should be present. An absent uterus and primary amenorrhea can be seen in Müllerian agenesis and androgen insensitivity syndrome.

**(Choice B)** Turner syndrome patients have normal female external genitalia. Ambiguous external genitalia can be seen in 46,XX patients with congenital adrenal hyperplasia.

**(Choice D)** Fibrotic fallopian tubes are not seen in Turner syndrome but are sometimes seen in pelvic inflammatory disease.

**(Choice E)** Hirsutism and secondary amenorrhea can be seen in polycystic ovarian syndrome.

**(Choice F)** Vaginal agenesis results from absence or underdevelopment of the Müllerian ductal system (Müllerian agenesis). Although patients with Müllerian agenesis have primary amenorrhea, they will have normal palate and breast development.

### Educational objective:

Common manifestations of Turner syndrome include primary amenorrhea, short stature, a high arched palate, and widely spaced nipples. Primary amenorrhea occurs in these patients due to in utero degeneration of the ovarian follicles (gonadal dysgenesis).

### References



A 23-year-old primigravida woman vaginally delivers a 3600-g (7 lb 15 oz) girl after a protracted labor. The patient sustains second-degree laceration and repair is planned. Prior to administering local anesthesia, the operator intravaginally palpates bony protrusions located posterolateral to the vaginal sidewalls that are distinct from the rest of the pelvic sidewall. A firm band can also be palpated running medially and posteriorly from the bony prominence to the sacrum. Anesthetic agent is injected around the bony prominence. Which of the following nerves is blocked by the injection?

- ☐ A. Genitofemoral
- ☐ B. Iliohypogastric
- ☐ C. Inferior gluteal
- ☐ D. Lateral femoral cutaneous
- ☐ E. Obturator
- ☐ F. Pudendal

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A 23-year-old primigravida woman vaginally delivers a 3600-g (7 lb 15 oz) girl after a protracted labor. The patient sustains second-degree laceration and repair is planned. Prior to administering local anesthesia, the operator intravaginally palpates bony protrusions located posterolateral to the vaginal sidewalls that are distinct from the rest of the pelvic sidewall. A firm band can also be palpated running medially and posteriorly from the bony prominence to the sacrum. Anesthetic agent is injected around the bony prominence. Which of the following nerves is blocked by the injection?

- ☐ A. Genitofemoral (4%)
- ☐ B. Iliohypogastric (2%)
- ☐ C. Inferior gluteal (1%)
- ☐ D. Lateral femoral cutaneous (0%)
- ☐ E. Obturator (3%)
- ☒ F. Pudendal (88%)







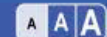
### Pelvic innervation

Nerve	Origin	Function
Pudendal	S2-S4	Sensory: Perineum Motor: Urethral & anal sphincters
Lateral femoral cutaneous	L2-L3	Sensory: Anterior & lateral thigh
Inferior gluteal	L5-S2	Motor: Gluteus maximus
Genitofemoral	L1-L2	Sensory: Scrotum/labia majora, medial thigh
Obturator	L3-L4	Sensory: Medial thigh Motor: Adduction
Iliohypogastric	T12-L1	Sensory: Suprapubic

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Local anesthesia may be administered if a woman has progressed too far in labor to receive epidural anesthesia. This patient is receiving a **pudendal nerve** (PN) block for perineal laceration repair. The PN is





Local anesthesia may be administered if a woman has progressed too far in labor to receive epidural anesthesia. This patient is receiving a **pudendal nerve (PN)** block for perineal laceration repair. The PN is derived from the **S2-S4** nerve roots and provides sensory innervation to the **perineum and genitals**, as well as motor innervation to the sphincter urethrae and the external anal sphincter.

Important landmarks for a **PN block** include the **ischial spines** and **sacrospinous ligament**. The ischial spines are bony protrusions located posterolateral to the vaginal sidewall. The sacrospinous ligament is a firm band that runs medially and posteriorly from the ischial spine to the sacrum. When administering a PN block, the ischial spines should be palpated intravaginally, and the anesthetic should be injected medially in very close proximity to the ischial spine through the sacrospinous ligament.

Other important structures include the **internal pudendal artery and inferior gluteal artery**, which run medial to the PN. Inadvertent injection into these vessels can lead to **hematoma** or arrhythmia from intravascular infiltration of local anesthetics (eg, lidocaine).

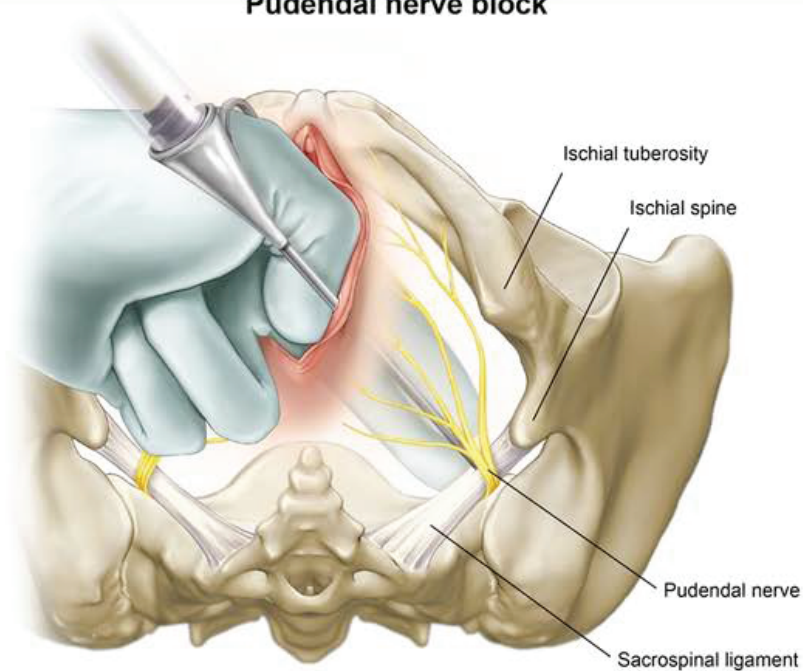
**(Choices A, B, and E)** Pelvic surgery carries the risk of several other **neuropathies**:

- The genitofemoral nerve courses along the anterior surface of the psoas muscle. Its branches innervate the scrotum/labia majora and the medial thigh. Injury from abdominal retractors during



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## Pudendal nerve block



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(Choices A, B, and E) Pelvic surgery carries the risk of several other neuropathies.

- The genitofemoral nerve courses along the anterior surface of the psoas muscle. Its branches innervate the scrotum/labia majora and the medial thigh. Injury from abdominal retractors during laparotomy can lead to labial/scrotal anesthesia.
- The iliohypogastric nerve innervates the suprapubic skin. Injury during closure of Pfannenstiel skin incisions (eg, cesarean section) can result in burning pain and paresthesias.
- The obturator nerve provides motor and sensory innervation to the medial thigh. Injury during retroperitoneal pelvic lymph node dissection can result in loss of medial thigh sensation and ability to adduct the thigh.

**(Choice C)** The inferior gluteal nerve innervates the gluteus maximus. Injury during hip surgery can impair hip extension.

**(Choice D)** The **lateral femoral cutaneous nerve** courses deep to the inguinal ligament to innervate the anterolateral thigh skin. It is commonly injured during hyperflexion of the thighs in the lithotomy position for pelvic surgery or a vaginal delivery. Complications include anterior and lateral thigh numbness (eg, meralgia paresthetica).

### Educational objective:

A pudendal nerve block is performed by injecting an anesthetic intravenously medial to the ischial spine.

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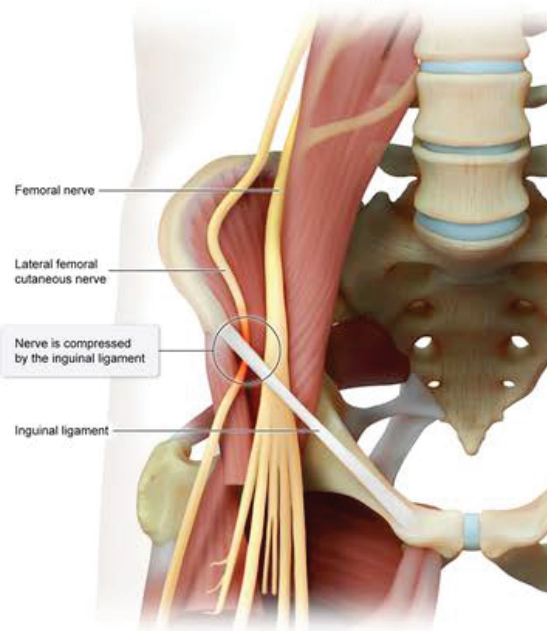
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(Choices A, B, and E) Pelvic surgery carries the risk of several other neuropathies.

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Lateral femoral cutaneous nerve &amp; meralgia paresthetica



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### Educational objective:

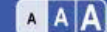
A pudendal nerve block is performed by injecting an anesthetic intravaginally, medial to the ischial spine, through the sacrospinous ligament. This provides anesthesia to most of the perineum.

### References

- **Pudendal nerve block for vaginal birth.**







A 44-year-old woman, gravida 2, para 2, is being evaluated after having several episodes of painless postcoital bleeding. She emigrated from Guatemala 5 years ago and has not received any preventative health care. The patient is married and gave birth to two girls via vaginal delivery at home in Guatemala. Her menstrual periods have been regular, and she uses barrier contraceptives. Speculum examination reveals an ulcerative lesion at the external cervical os. Cervical biopsy shows malignant squamous cells invading the underlying stroma. Further analysis of the malignant cells reveals that a double-stranded DNA virus, which encodes several proteins including E6 and E7, has integrated into the host genome. Which of the following is the most likely mechanism by which these viral proteins are involved in this patient's condition?

- ☐ A. Constitutive activation of a cytoplasmic signal transducer protein
- ☒ B. Constitutive activation of a transmembrane growth factor receptor
- ☐ C. Inactivation of DNA repair proteins
- ☐ D. Inhibition of cell cycle regulatory proteins
- ☐ E. Enhancement of growth factor synthesis and secretion





postcoital bleeding. She emigrated from Guatemala 5 years ago and has not received any preventative health care. The patient is married and gave birth to two girls via vaginal delivery at home in Guatemala. Her menstrual periods have been regular, and she uses barrier contraceptives. Speculum examination reveals an ulcerative lesion at the external cervical os. Cervical biopsy shows malignant squamous cells invading the underlying stroma. Further analysis of the malignant cells reveals that a double-stranded DNA virus, which encodes several proteins including E6 and E7, has integrated into the host genome. Which of the following is the most likely mechanism by which these viral proteins are involved in this patient's condition?

- ☐ A. Constitutive activation of a cytoplasmic signal transducer protein (2%)
- ☐ B. Constitutive activation of a transmembrane growth factor receptor (2%)
- ☐ C. Inactivation of DNA repair proteins (6%)
- ☒ D. Inhibition of cell cycle regulatory proteins (85%)
- ☐ E. Enhancement of growth factor synthesis and secretion (2%)







This patient has biopsy-confirmed squamous cell **carcinoma of the cervix** as a result of **human papillomavirus (HPV)** infection. HPV is a small double-stranded DNA virus with multiple genotypes. High-risk subtypes 16 and 18 are most commonly identified in cervical cancers.

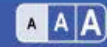
The oncogenic capability of HPV is dependent on its ability to integrate into the host genome and subsequently produce **viral proteins E6 and E7**, which interact with cell cycle regulatory proteins **p53 and Rb**, respectively. E6 binds p53, leading to its ubiquitination and subsequent proteasomal degradation. Without p53, the cell is unable to halt cell growth to repair damaged DNA or trigger apoptosis when DNA is damaged beyond repair. Similarly, E7 binds Rb and displaces bound transcription factors, promoting unregulated DNA replication and cyclin-mediated cell cycling. The collective effects of E6 and E7 lead to **inhibition of cell cycle regulation** and evasion of apoptosis, consequently increasing malignant potential.

**(Choice A)** *RAS* and *BRAF* are proto-oncogenes that code for cytoplasmic signal transducer proteins, which upregulate cellular proliferation and differentiation when activated. Mutations causing constitutive activation of these proteins are linked to development of pancreatic cancer (Ras) and malignant melanomas (BRAF).

**(Choice B)** Mutations resulting in upregulation of the epithelial growth factor receptor (*EGFR*) gene have







melanomas (BRAF).

**(Choice B)** Mutations resulting in upregulation of the epithelial growth factor receptor (*EGFR*) gene have been implicated in the development of solid tumors (eg, colon, breast, lung).

**(Choice C)** MSH2 is a DNA mismatch repair protein encoded by the *MSH2* gene, which leads to ineffective DNA repair when inactivated. This is the pathogenic basis of hereditary nonpolyposis colorectal cancer (HNPCC).

**(Choice E)** Platelet derived growth factor (PDGF) activity is essential for normal development of the central nervous system during the embryonic period. Upregulation of PDGF synthesis and corresponding receptor activation are responsible for the malignant transformation of glial cells in glioblastoma.

### Educational objective:

Human papillomavirus (HPV) oncogenicity relies on the inhibitory effects of viral proteins E6 and E7 on cell cycle regulatory proteins p53 and Rb. This allows cells infected with HPV to undergo unchecked cellular proliferation and evasion of apoptosis, promoting genomic instability and malignant transformation.

### References

- The role of HPV E6 and E7 oncoproteins in HPV-associated cervical carcinogenesis.





A 24-year-old woman comes to the office due to copious green vaginal discharge and burning with urination for 3 days. The patient had a yeast infection a year ago, which was treated with over-the-counter medication. She has recently become sexually active with a new partner and occasionally uses condoms. Physical examination shows a yellow-green, frothy vaginal discharge and diffuse vaginal erythema but no lesions. The uterus is anteverted with no cervical motion tenderness. Which of the following is the best test to confirm the diagnosis in this patient?

- ☐ A. Cervical cytology
- ☐ B. Gram stain
- ☐ C. Potassium hydroxide testing
- ☐ D. Urine culture
- ☐ E. Vaginal pH
- ☐ F. Wet mount saline microscopy

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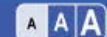


A 24-year-old woman comes to the office due to copious green vaginal discharge and burning with urination for 3 days. The patient had a yeast infection a year ago, which was treated with over-the-counter medication. She has recently become sexually active with a new partner and occasionally uses condoms. Physical examination shows a yellow-green, frothy vaginal discharge and diffuse vaginal erythema but no lesions. The uterus is anteverted with no cervical motion tenderness. Which of the following is the best test to confirm the diagnosis in this patient?

- ☐ A. Cervical cytology (3%)
- ☐ B. Gram stain (6%)
- ☐ C. Potassium hydroxide testing (13%)
- ☐ D. Urine culture (3%)
- ☐ E. Vaginal pH (5%)
- ☒ F. Wet mount saline microscopy (68%)







The most likely cause of this patient's abnormal vaginal discharge is ***Trichomonas vaginalis***, a sexually transmitted infection that often presents with a **malodorous, thin, frothy, yellow-green vaginal discharge**. The trichomonads infect the squamous epithelium of the vagina, resulting in vulvovaginal inflammation and subsequent vulvar pruritus, dyspareunia, **vulvovaginal erythema**, and discharge.

**Wet mount saline microscopy** of **trichomoniasis** typically shows characteristic **motile, flagellated protozoans**. Nucleic acid amplification testing can also be performed and is the gold standard. Treatment of the patient and the patient's sexual partners is with metronidazole.

**(Choice A)** Cervical cytology (ie, Pap test) is a screening test for cervical cancer. Most patients with high-grade cervical lesions or cervical cancer are asymptomatic; patients with symptoms typically present with postcoital bleeding or a mucopurulent cervical discharge with an associated cervical lesion.

**(Choice B)** ***Neisseria gonorrhoeae*** is a common sexually transmitted infection that may present with mucopurulent (not frothy) vaginal discharge originating from an inflamed cervix. A Gram stain may show gram-negative diplococci in polymorphonuclear leukocytes. Gram staining is not performed for *T vaginalis* because the process often changes the organism's shape, making it difficult to identify.

**(Choice C and E)** pH and whiff tests can be used to diagnose bacterial vaginosis, which typically presents with thin, off-white, malodorous discharge with no associated vaginitis. In bacterial vaginosis, the addition



because the process often changes the organism's shape, making it difficult to identify.

**(Choice C and E)** pH and whiff tests can be used to diagnose bacterial vaginosis, which typically presents with thin, off-white, malodorous discharge with no associated vaginitis. In bacterial vaginosis, the addition of potassium hydroxide (KOH) to the vaginal discharge releases amines, causing a characteristic odor (eg, positive whiff test). Vaginal pH is elevated in both bacterial vaginosis and trichomonas infection; therefore, pH testing is not specific for diagnosis.

**(Choice D)** Urine culture is used to diagnose urinary tract infections, which can present with dysuria; however, patients do not have associated vaginal discharge.

**Educational objective:**

*Trichomonas vaginalis* is a sexually transmitted motile protozoan which can be seen on wet mount microscopy of vaginal discharge. It presents with yellow-green, frothy vaginal discharge and vulvovaginal erythema.

Microbiology  
Subject

Female Reproductive System & Breast  
System

Vulvovaginitis  
Topic

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An autopsy was performed on a 17-year-old girl after a fatal motor vehicle collision. Her ovaries appear small and underdeveloped on gross examination. Light microscopic examination shows ovaries primarily composed of connective tissue with no follicles. Which of the additional abnormalities is most likely to be found on postmortem examination?

- ☐ A. Bicuspid aortic valve
- ☐ B. Inspissated pancreatic ducts
- ☐ C. Lens displacement
- ☐ D. Mitral valve prolapse
- ☐ E. Vaginal adenosis

Submit







An autopsy was performed on a 17-year-old girl after a fatal motor vehicle collision. Her ovaries appear small and underdeveloped on gross examination. Light microscopic examination shows ovaries primarily composed of connective tissue with no follicles. Which of the additional abnormalities is most likely to be found on postmortem examination?



- ☒ A. Bicuspid aortic valve (85%)
- ☐ B. Inspissated pancreatic ducts (1%)
- ☐ C. Lens displacement (2%)
- ☐ D. Mitral valve prolapse (5%)
- ☐ E. Vaginal adenosis (5%)

Correct



85%

Answered correctly



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Time Spent



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Explanation

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The ovaries described in the vignette are the streak ovaries of Turner syndrome (TS). Patients with TS have normal ovarian development during fetal life. However, lack of the paternal X chromosome causes loss of ovarian follicles by age 2, as well as a karyotype of 45, X. At puberty, patients with TS usually have normal pubic hair but no breasts or menses due to ovarian failure. **Premature ovarian failure** is characterized by **high LH and FSH levels**, and TS is one of the most common causes.

Patients with TS also have several extragonadal abnormalities. Short stature, shield chest (broad, with widely spaced nipples), and webbed neck (broad neck with low hairline) comprise the appearance of these patients. Lymphedema may be seen at any age, including neonates. **Bicuspid aortic valve** (20%-30%) is the most common cardiovascular anomaly; other common defects include **coarctation of the aorta** (3%-10%) and aortic root dilation with an increased risk of aortic dissection in adulthood.

**(Choice B)** Pancreatic insufficiency occurs in patients with cystic fibrosis due to obstructed, inspissated pancreatic ducts.

**(Choices C and D)** Mitral valve prolapse and lens displacement are seen in patients with Marfan syndrome. These patients are also at risk for aortic root dilation and aortic dissection.

**(Choice E)** Vaginal adenosis is replacement of the vaginal squamous epithelium with glandular columnar



pancreatic ducts.

**(Choices C and D)** Mitral valve prolapse and lens displacement are seen in patients with Marfan syndrome. These patients are also at risk for aortic root dilation and aortic dissection.

**(Choice E)** Vaginal adenosis is replacement of the vaginal squamous epithelium with glandular columnar epithelium. It occurs in the female children of women exposed to diethylstilbestrol (DES) during pregnancy. Vaginal adenosis is a precursor of clear cell adenocarcinoma of the vagina.

### Educational objective:

Streak ovaries, amenorrhea, and infertility are the gynecologic complications of Turner syndrome (TS). In addition, patients with TS usually have short stature, webbed neck, shield chest, and low posterior hairline. Bicuspid aortic valve is the most common cardiac comorbidity.

### References

- [Turner syndrome: diagnosis and management.](#)
- [Aortic valve disease in Turner syndrome.](#)

Genetics      Female Reproductive System & Breast      Turner syndrome  
Subject      System      Topic

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A 30-year-old woman comes to the office for evaluation of irregular menses. The patient has had increasingly irregular menses over the past 6 months, and hot flushes and unintentional weight loss for the past few months. She has also had intermittent lower abdominal pain that is usually worse after increased physical activity. The patient has no chronic medical conditions and takes no daily medications. Vital signs are normal. The abdomen is nontender. A pelvic examination shows a left adnexal mass and a small uterus. TSH is low and a urine pregnancy test is negative. Pelvic ultrasound reveals a 6-cm left ovarian mass. The mass is surgically removed, and gross examination of the specimen shows a cystic lesion with an oily substance. Which of the following cell types is the most likely source of the neoplasm in this patient?

- ☐ A. Ectopic endometrial cells
- ☐ B. Germ cells
- ☒ C. Granulosa cells
- ☐ D. Ovarian fibroblasts
- ☐ E. Theca cells



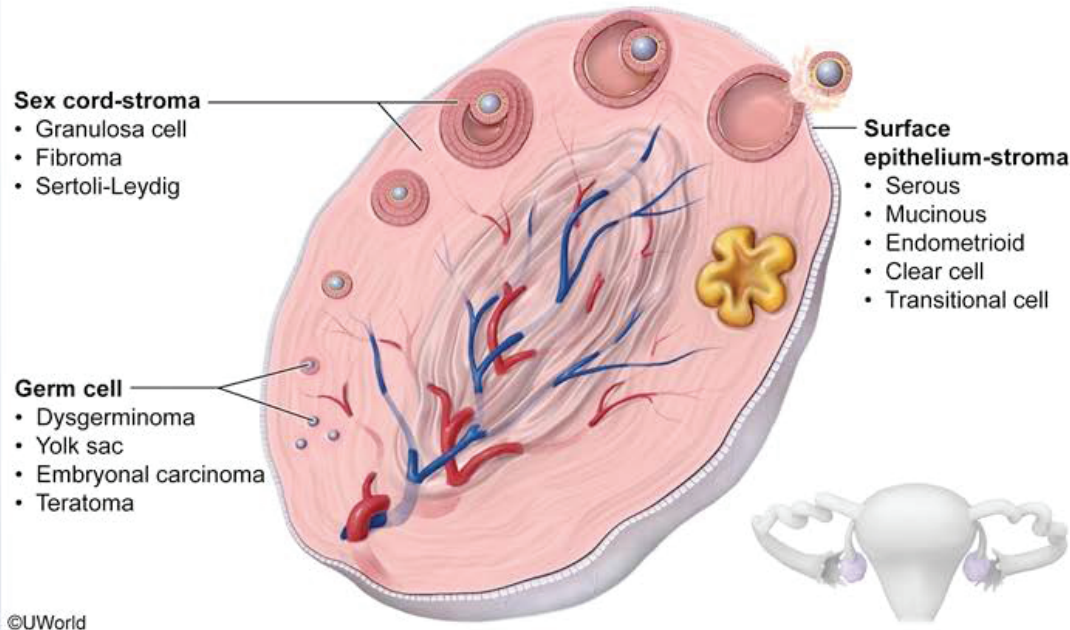


increasingly irregular menses over the past 6 months, and not flushes and unintentional weight loss for the past few months. She has also had intermittent lower abdominal pain that is usually worse after increased physical activity. The patient has no chronic medical conditions and takes no daily medications. Vital signs are normal. The abdomen is nontender. A pelvic examination shows a left adnexal mass and a small uterus. TSH is low and a urine pregnancy test is negative. Pelvic ultrasound reveals a 6-cm left ovarian mass. The mass is surgically removed, and gross examination of the specimen shows a cystic lesion with an oily substance. Which of the following cell types is the most likely source of the neoplasm in this patient?

- ☐ A. Ectopic endometrial cells (8%)
- ☒ B. Germ cells (42%)
- ☐ C. Granulosa cells (22%)
- ☐ D. Ovarian fibroblasts (4%)
- ☐ E. Theca cells (21%)



### Categorization of ovarian tumors



**Ovarian tumors** are classified based on their **predominant cell type**, which determines their classic





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**Ovarian tumors** are classified based on their **predominant cell type**, which determines their classic clinical symptoms and gross appearance. Ovarian tumor types include:

- Surface epithelial-stroma: composed of cells that support the normal ovarian structure for ovulation (eg, serous, mucinous epithelial cells).
- Sex cord-stroma: composed of cells that support and surround the oocyte. These cells secrete sex hormones including estrogen (granulosa cells) and testosterone (Sertoli-Leydig cells).
- Germ cell: composed of cells that can develop into an embryo or placenta. These tumors are composed of varying amounts of germ layers (ie, endoderm, mesoderm, ectoderm), yolk sac, or placenta (eg, chorion). They often have associated hormonal activity (eg, increased hCG, alpha fetoprotein).

This patient's unintentional weight loss, hot flushes, irregular menses, and low TSH level are consistent with **thyrotoxicosis** (ie, abnormally high circulating thyroid hormone levels). In the setting of an adnexal mass, this presentation is classic for **struma ovarii**, an ovarian **germ cell tumor** composed of >50% mature thyroid tissue (derived from the **endoderm**) that can secrete thyroid hormone. On gross





mass, this presentation is classic for **struma ovarii**, an ovarian **germ cell tumor** composed of >50% mature thyroid tissue (derived from the **endoderm**) that can secrete thyroid hormone. On gross examination, struma ovarii typically appears as an oily (eg, sebaceous) cystic mass. Microscopic examination reveals **thyroid follicles** filled with colloid and surrounded by ovarian stroma.

**(Choice A)** **Endometriomas** occur when ectopic endometrial tissue and old blood collect in the ovary. Patients can have lower abdominal pain; however, they typically have regular menses. In addition, endometriosis is not associated with hot flashes, weight loss, or abnormal TSH levels.

**(Choice C)** Granulosa cell tumors are a type of sex cord–stroma tumor that secrete estrogen and inhibin, thereby suppressing FSH release and causing irregular menses. They do not secrete thyroid hormone and therefore do not cause thyrotoxicosis.

**(Choice D)** **Ovarian fibromas** are sex cord–stroma tumors that arise from ovarian fibroblasts, which have no endocrine activity and therefore do not affect TSH levels. Fibromas are typically solid, not cystic.

**(Choice E)** Ovarian thecomas are benign sex cord–stroma tumors composed of cells histologically similar to thecal cells. Therefore, thecomas typically increase circulating estrogen (causing abnormal uterine bleeding) but do not cause thyrotoxicosis.







Patients can have lower abdominal pain; however, they typically have regular menses. In addition,

endometriosis is not associated with hot flashes, weight loss, or abnormal TSH levels.

**(Choice C)** Granulosa cell tumors are a type of sex cord–stroma tumor that secrete estrogen and inhibin, thereby suppressing FSH release and causing irregular menses. They do not secrete thyroid hormone and therefore do not cause thyrotoxicosis.

**(Choice D)** Ovarian fibromas are sex cord–stroma tumors that arise from ovarian fibroblasts, which have no endocrine activity and therefore do not affect TSH levels. Fibromas are typically solid, not cystic.

**(Choice E)** Ovarian thecomas are benign sex cord–stroma tumors composed of cells histologically similar to thecal cells. Therefore, thecomas typically increase circulating estrogen (causing abnormal uterine bleeding) but do not cause thyrotoxicosis.

### Educational objective:

Struma ovarii is an ovarian germ cell tumor composed of >50% mature thyroid tissue that can secrete thyroid hormone. Therefore, struma ovarii can be a rare cause of thyrotoxicosis (eg, weight loss, irregular menses, low TSH level).

Pathophysiology

Female Reproductive System & Breast

Ovarian cancer

Subject

System

Topic







A 23-year-old woman comes to the emergency department for evaluation of right lower abdominal pain and bloody vaginal discharge. Her symptoms began this morning and are progressively worsening. She is sexually active with 1 male partner. The patient takes no daily medications and has no known drug allergies. Her last menstrual period was 5 weeks ago, and she has never been pregnant. Blood pressure is 112/70 mm Hg while supine and 96/60 mm Hg while standing. The patient is tachycardic and ill appearing. On pelvic examination, the uterus is small and mobile, and there is right adnexal tenderness. Laboratory results are as follows:

Complete blood count

Hemoglobin 11 g/dL

Platelets 200,000/mm<sup>3</sup>

Leukocytes 9,000/mm<sup>3</sup>

Urine  $\beta$ -hCG positive

This patient's clinical presentation is most likely due to a prior infection with which of the following pathogens?





Platelets 200,000/mm<sup>3</sup>

Leukocytes 9,000/mm<sup>3</sup>

Urine  $\beta$ -hCG positive

This patient's clinical presentation is most likely due to a prior infection with which of the following pathogens?

- ☐ A. *Escherichia coli*
- ☐ B. *Gardnerella vaginalis*
- ☐ C. Herpes simplex virus
- ☐ D. Human papillomavirus
- ☐ E. *Neisseria gonorrhoeae*
- ☐ F. *Treponema pallidum*
- ☐ G. *Trichomonas vaginalis*



Leukocytes 9,000/mm<sup>3</sup>Urine  $\beta$ -hCG positive

This patient's clinical presentation is most likely due to a prior infection with which of the following pathogens?

- ☐ A. *Escherichia coli* (3%)
- ☐ B. *Gardnerella vaginalis* (1%)
- ☐ C. Herpes simplex virus (0%)
- ☐ D. Human papillomavirus (4%)
- ☒ E. *Neisseria gonorrhoeae* (85%)
- ☐ F. *Treponema pallidum* (2%)
- ☐ G. *Trichomonas vaginalis* (2%)

Correct

85%



43 secs



12/03/2020

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This patient with lower abdominal pain, bloody vaginal discharge, hemodynamic instability (eg, tachycardia, orthostatic hypotension), and a positive pregnancy test most likely has a **ruptured ectopic pregnancy**. Ectopic pregnancies occur due to extrauterine pregnancy implantation, typically in the ampulla of the **fallopian tube**.

The most common risk factor for ectopic pregnancy is **tubal scarring**, which impedes normal migration of the fertilized embryo through the fallopian tube and into the uterus. Tubal scarring usually occurs due to **prior upper genital tract infection** (ie, **pelvic inflammatory disease** [PID]) from either ***Neisseria gonorrhoeae*** or ***Chlamydia trachomatis***. Both pathogens cause cervicitis, which compromises the cervix barrier and allows vaginal bacteria to ascend into the normally sterile upper genital tract, resulting in tubal inflammation and scarring.

**(Choice A)** *Escherichia coli*, an enteric bacteria, can ascend the urethra to cause a urinary tract infection. Although *E coli* may be found in the vagina, it does not commonly cause PID in premenopausal women.

**(Choices B and G)** *Gardnerella vaginalis* (bacterial vaginosis) and *Trichomonas vaginalis* (trichomoniasis) can cause vaginal discharge due to lower genital tract inflammation (ie, **vaginitis**). Neither is associated with increased risk of ectopic pregnancy.

**(Choices C and D)** Herpes simplex virus (HSV) and human papillomavirus (HPV) typically cause lower





Mark

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Full Screen

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Lab Values

Notes

Calculator

Reverse Color

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Settings

Although *E coli* may be found in the vagina, it does not commonly cause PID in premenopausal women.

**(Choices B and G)** *Gardnerella vaginalis* (bacterial vaginosis) and *Trichomonas vaginalis* (trichomoniasis) can cause vaginal discharge due to lower genital tract inflammation (ie, **vaginitis**). Neither is associated with increased risk of ectopic pregnancy.

**(Choices C and D)** Herpes simplex virus (HSV) and human papillomavirus (HPV) typically cause lower genital tract disease. HSV causes multiple small, vesicular genital ulcers and HPV causes genital warts or cervical/vaginal/perianal neoplasia. Neither causes upper genital tract infection or inflammation; therefore, neither is associated with ectopic pregnancy.

**(Choice F)** *Treponema pallidum* infection (ie, syphilis) usually begins in the lower genital tract as a single, painless genital chancre (ie, the transmission site). However, it does not cause PID.

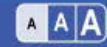
### Educational objective:

A ruptured ectopic pregnancy can cause abdominal pain, vaginal bleeding, and hemodynamic instability. A common risk factor is tubal scarring from a prior upper genital tract infection (ie, pelvic inflammatory disease) due to *Neisseria gonorrhoeae* or *Chlamydia trachomatis*.

### References

- **Current knowledge of the aetiology of human tubal ectopic pregnancy.**





A 39-year-old woman, gravida 2, para 2, is evaluated in the hospital after a total abdominal hysterectomy for symptomatic uterine fibroids. Hysterectomy was performed due to a history of heavy menses, abdominal fullness, and urinary incontinence. The largest fibroid, measuring 8 cm in diameter, was located in the lower aspect of the uterus at the level of the cardinal ligaments, compressing the bladder anteriorly. The patient has no other medical problems and no prior surgeries. Postoperatively, she has a fever and right-sided back pain. She has been able to urinate without any difficulty. Injury to which of the following structures is the most likely explanation for this patient's postoperative symptoms?

- ☐ A. Bladder
- ☐ B. External iliac artery
- ☐ C. Ovarian artery
- ☐ D. Ureter
- ☐ E. Uterine artery

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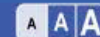


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A 39-year-old woman, gravida 2, para 2, is evaluated in the hospital after a total abdominal hysterectomy for symptomatic uterine fibroids. Hysterectomy was performed due to a history of heavy menses, abdominal fullness, and urinary incontinence. The largest fibroid, measuring 8 cm in diameter, was located in the lower aspect of the uterus at the level of the cardinal ligaments, compressing the bladder anteriorly. The patient has no other medical problems and no prior surgeries. Postoperatively, she has a fever and right-sided back pain. She has been able to urinate without any difficulty. Injury to which of the following structures is the most likely explanation for this patient's postoperative symptoms?

- ☐ A. Bladder (2%)
- ☐ B. External iliac artery (3%)
- ☐ C. Ovarian artery (10%)
- ☒ D. Ureter (63%)
- ☐ E. Uterine artery (19%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom

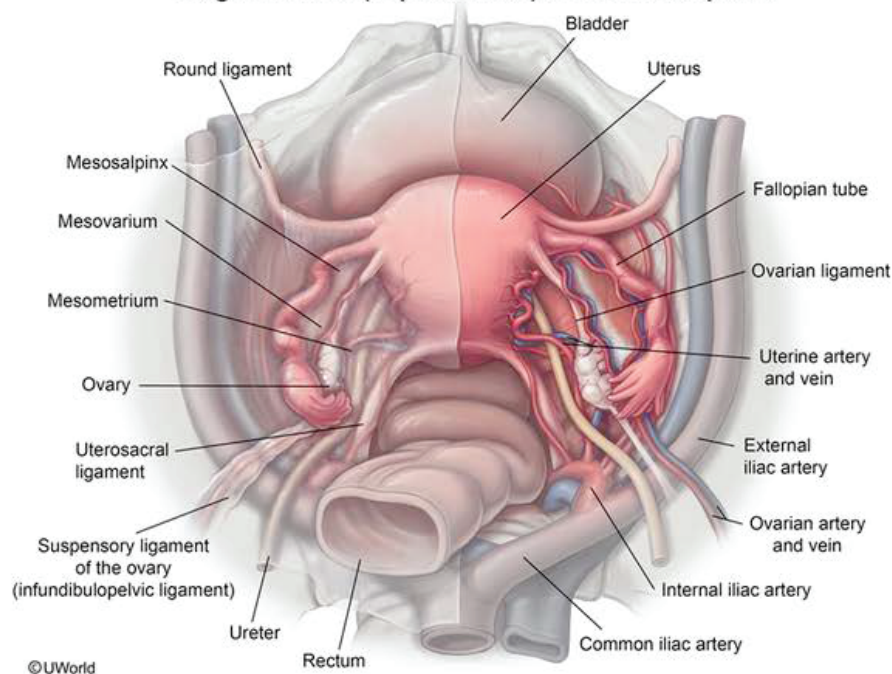


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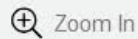
Bladder

## Exhibit Display

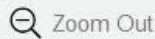
## Surgeon's view (superior view) of the female pelvis



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Zoom In



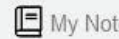
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My Notebook

This patient has a right ureteral injury, a rare but serious complication of pelvic surgery presenting with

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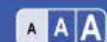
Feedback



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End Block



Ureter

Rectum

Common iliac artery

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This patient has a right **ureteral injury**, a rare but serious complication of pelvic surgery presenting with **flank pain** and **fever**. The ureter is a retroperitoneal structure that arises from the renal pelvis and enters the trigone at the posterior aspect of the urinary bladder, with equal proportions in the abdomen and pelvis. The pelvic portion starts at the level of the pelvic brim, and courses medially and anteriorly to the bifurcation of the common iliac arteries. Then, the ureter passes along the lateral pelvic sidewall posterior to the ovarian vessels to dive under the uterine vessels ("**water under the bridge**"= ureter carrying water, the uterine vessels signifying the bridge). Finally, it runs along the anterolateral surface of the cervix at the level of the internal os to enter the bladder trigone.

The ureter is most vulnerable to injury during a **hysterectomy**, where the damage can occur at the point of ligation of the uterine vessels and closure of the lateral aspects of the vaginal cuff. This patient was at increased risk for injury secondary to a large fibroid close to the course of the distal ureter. A ureteral obstruction injury with a suture leads to flank pain due to distention of the proximal ureter with urine. A transection injury of the ureter causes localized leakage of urine as well as flank pain. Since the **second ureter is uninjured**, patients are able to **void (urinate) normally**. Bilateral ureteral injury is extremely unlikely and would result in anuria and bilateral flank pain.







unlikely and would result in anuria and bilateral flank pain.

**(Choice A)** The bladder can be injured in a hysterectomy during its separation from the lower aspect of the uterus and cervix. This patient is at risk for bladder injury given the distorted uterine anatomy, but a bladder injury would present with urinary symptoms (dysuria, hematuria, or anuria) and not unilateral flank pain.

**(Choices B and C)** The external iliac and ovarian arteries are not manipulated during a hysterectomy and are not typically at risk for injury. The ovarian vessels are ligated when an oophorectomy is performed, and the point of ligation is a potential area for ureteral injury. However, this patient did not undergo an oophorectomy.

**(Choice E)** The uterine vessels, which contain the main uterine blood supply, are ligated during a hysterectomy. Ligation may be difficult in the setting of a large fibroid. Unrecognized insufficient ligation may lead to hemorrhage, which would present postoperatively as an acute abdomen with hypotension, tachycardia, and dizziness.

**Educational objective:**

The ureter can be injured during hysterectomy due to its close proximity to the uterine structures. The distal ureter may be severed during ligation of the uterine vessels because the ureter passes inferior and lateral to the uterine artery at the level of the internal cervical os prior to entering the bladder (eg, "water



are not typically at risk for injury. The ovarian vessels are ligated when an oophorectomy is performed, and the point of ligation is a potential area for ureteral injury. However, this patient did not undergo an oophorectomy.

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### Educational objective:

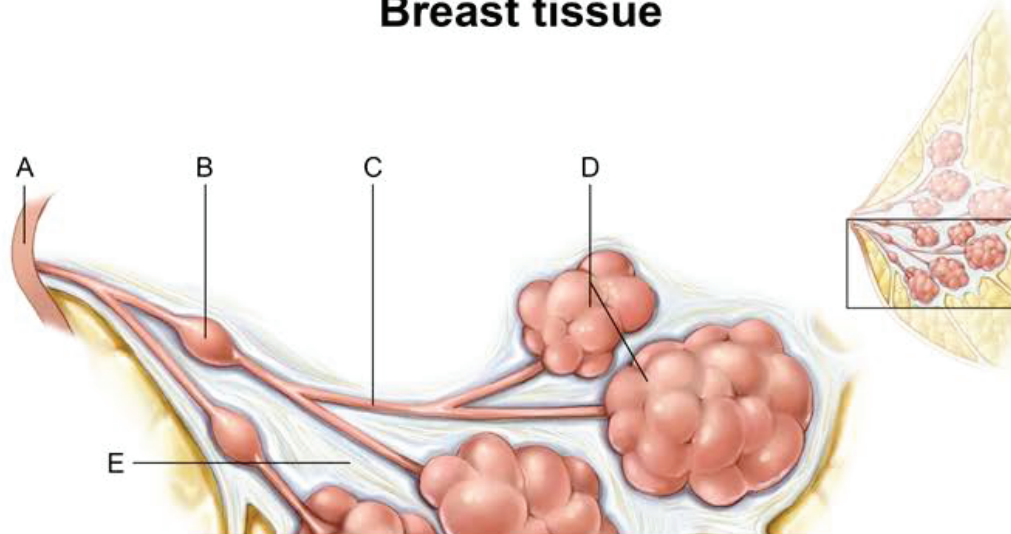
The ureter can be injured during hysterectomy due to its close proximity to the uterine structures. The distal ureter may be severed during ligation of the uterine vessels because the ureter passes inferior and lateral to the uterine artery at the level of the internal cervical os prior to entering the bladder (eg, "water under the bridge").

### References

- [Urinary tract injuries: recognition and management.](#)
- [Urinary tract injury during hysterectomy based on universal cystoscopy.](#)

A 50-year-old woman, gravida 0 para 0, comes to the office for a well visit. She has no family history of cancer. Breast examination is normal. The patient has a screening mammography that reveals microcalcifications. Due to this finding, she undergoes a breast biopsy. Histopathology reveals ducts distended by pleomorphic cells with prominent central necrosis. The lesion does not extend beyond the ductal basal membrane. Which of the following is most likely the origin of the lesion?

### Breast tissue





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www.ncbi.nlm.nih.gov/pubmed/18466808



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Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



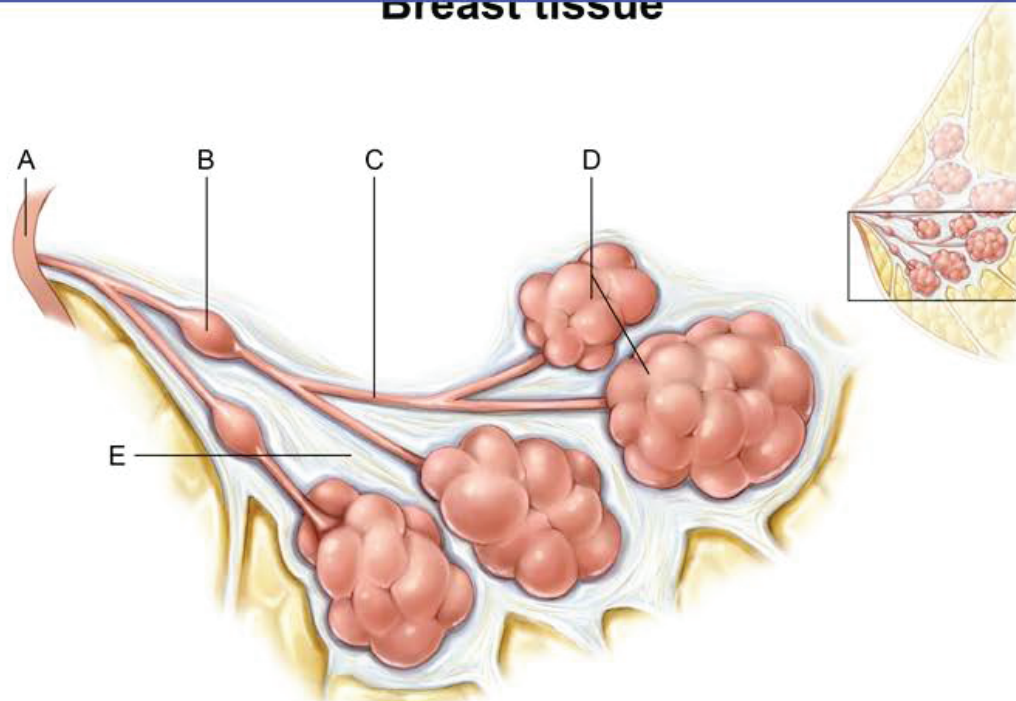
Text Zoom



Settings

## Exhibit Display

### Breast tissue



Zoom In

Zoom Out

Reset

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My Notebook

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E

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- ☐ A.A
- ☐ B.B
- ☐ C.C
- ☐ D.D
- ☐ E.E

**Submit**

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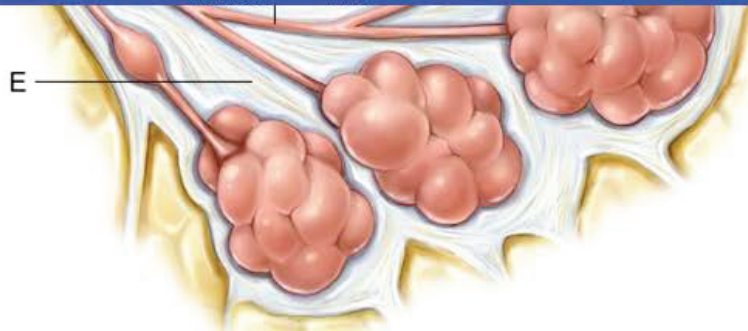


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E



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- ☐ A.A (1%)
- ☐ B.B (12%)
- ☒ C.C (68%)
- ☐ D.D (13%)
- ☐ E.E (3%)

Correct

68%  
Answered correctly

52 secs  
Time Spent

02/14/2021  
Last Updated

Block Time Remaining: 00:13:55

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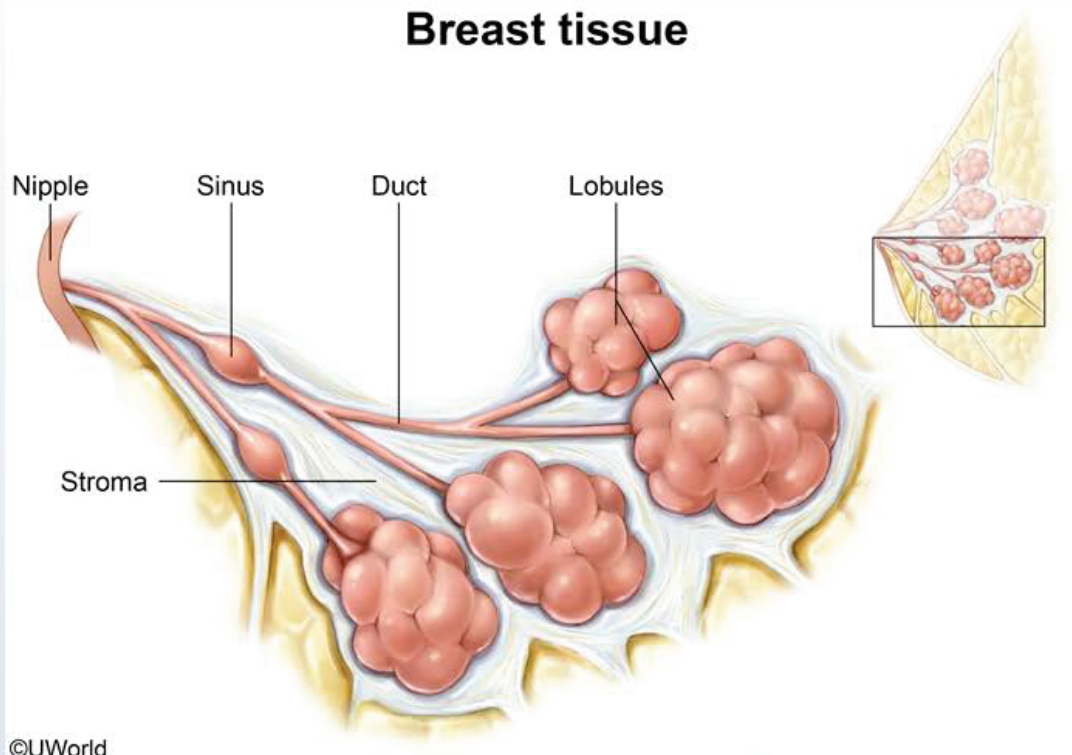
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## Breast tissue



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The breast is composed of subcutaneous tissue and breast tissue, the latter of which includes stromal and





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The breast is composed of subcutaneous tissue and breast tissue, the latter of which includes stromal and epithelial elements. Stroma constitutes the majority of breast volume in nonlactating women and consists of fibrous connective tissue. The epithelial elements of breast tissue proliferate during lactation and include branching ducts, which connect the lobules to sinuses that drain to the nipple.

As the name suggests, **ductal carcinoma in situ** (DCIS) arises from the breast ducts. It is a precursor to the most common type of breast cancer, invasive ductal carcinoma. Age and nulliparity are risk factors for breast cancer, and breastfeeding has a protective effect. DCIS is typically identified by biopsy after mammography screening shows **microcalcifications** in asymptomatic patients with normal breast examinations. [Histopathology](#) demonstrates ducts (black arrows) distended by pleomorphic cells with prominent **central necrosis** without extension beyond the ductal basement membrane. Spread of these malignant cells to the nipple through the duct system results in eczematous nipple changes and indicates [Paget disease](#) (**Choice A**).

(**Choice B**) The sinuses serve as collecting reservoirs for milk during lactation. A blockage of this area can cause a galactocele and eventually lead to a breast abscess.

(**Choice D**) Lobular breast tissue can give rise to lobular breast carcinoma that typically presents as







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

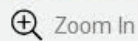
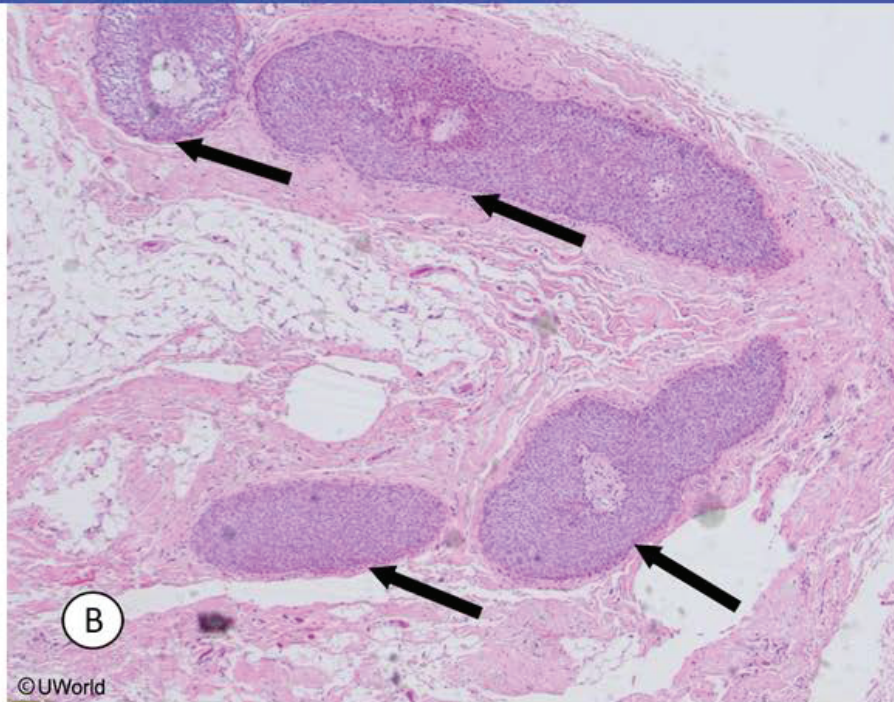


Text Zoom

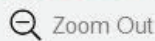


Settings

### Exhibit Display



Zoom In



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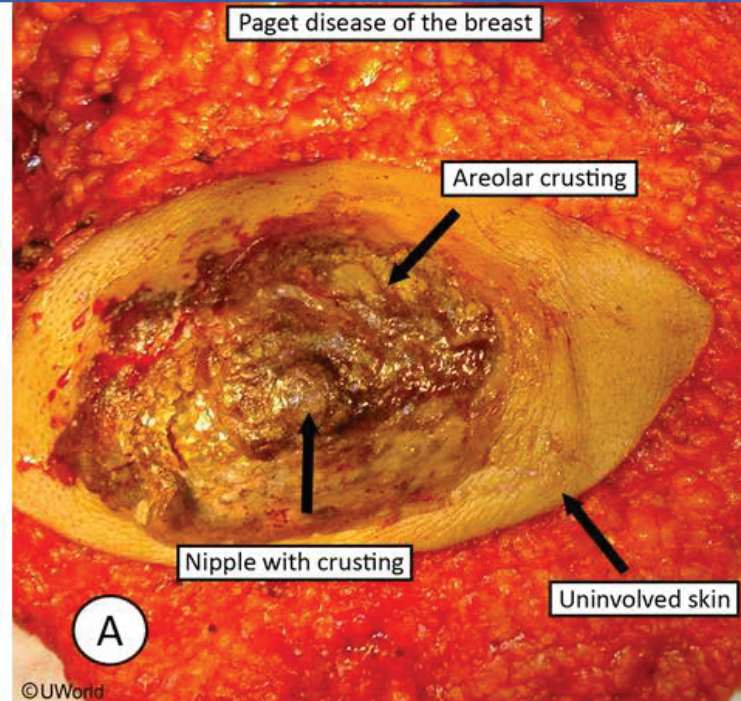


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End Block

Exhibit Display



Zoom In Zoom Out Reset New Existing My Notebook

(Choice D) Lobular breast tissue can give rise to lobular breast carcinoma that typically presents as

Block Time Remaining: 00:13:55

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malignant cells to the nipple through the duct system results in eczematous nipple changes and indicates

[Paget disease \(Choice A\).](#)

**(Choice B)** The sinuses serve as collecting reservoirs for milk during lactation. A blockage of this area can cause a galactocele and eventually lead to a breast abscess.

**(Choice D)** Lobular breast tissue can give rise to lobular breast carcinoma that typically presents as palpable breast masses with orderly rows of cells organized in [single file](#).

**(Choice E)** Phyllodes tumors arise from the breast stroma and can progress to malignancy. Histology shows disorderly, diffusely hypercellular connective tissue with cellular atypia and [leaf-like](#) projections (black arrow).

### Educational objective:

Ductal carcinoma in situ is characterized by ducts distended by pleomorphic cells with prominent central necrosis that do not penetrate the basement membrane. It is the precursor to invasive ductal carcinoma, the most common type of breast cancer.

### References

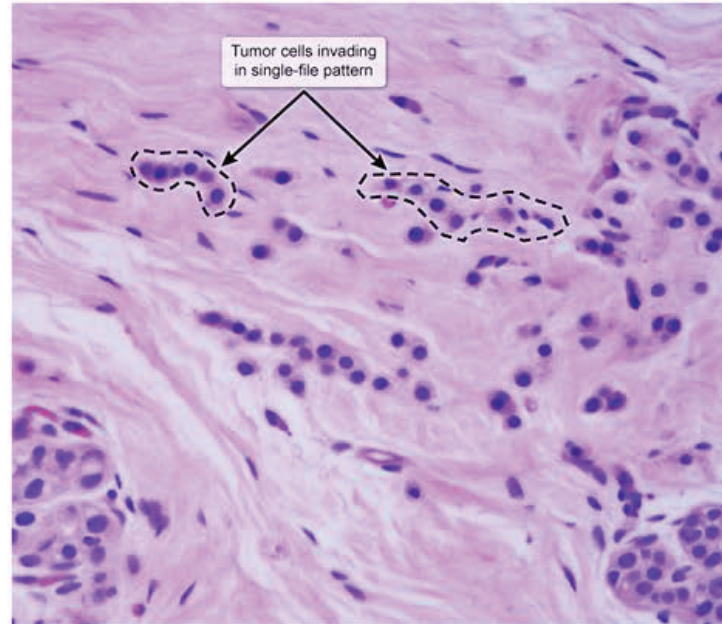
- [Progression from ductal carcinoma in situ to invasive breast cancer: revisited.](#)



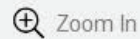
malignant cells to the nipple through the duct system results in eczematous nipple changes and indicates

## Exhibit Display

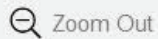
## Invasive lobular carcinoma of the breast



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Item 15 of 40

Question Id: 1057



Mark



Previous



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Reverse Color



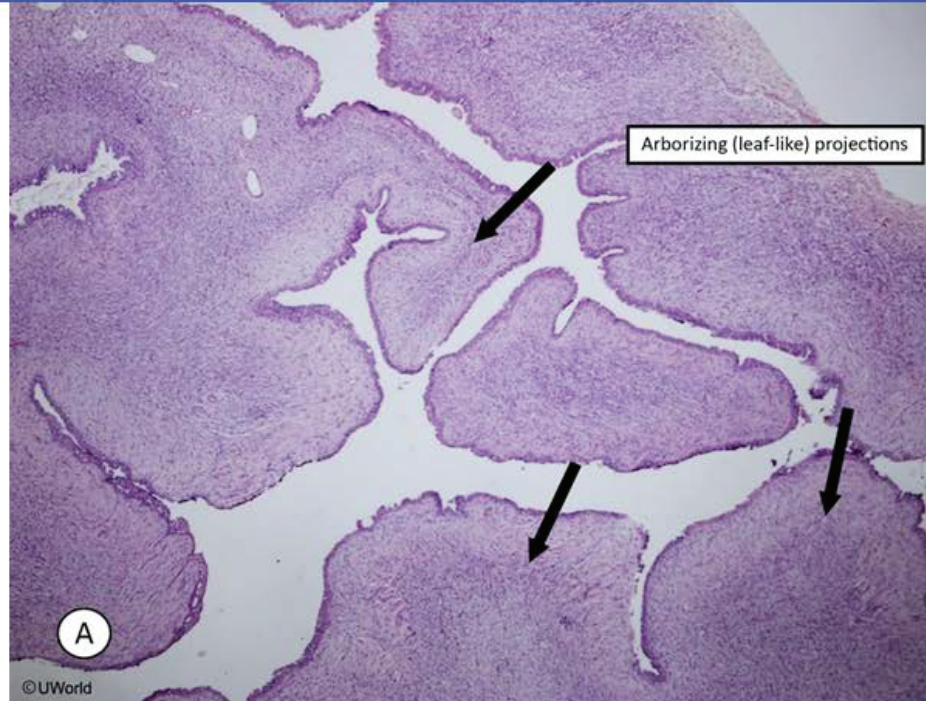
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malignant cells to the nipple through the duct system results in eczematous nipple changes and indicates

Exhibit Display



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Block Time Remaining: 00:13:55

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End Block



A 34-year-old woman comes to the office with bleeding from the right nipple. The patient has noticed blood staining her bra on several occasions over the past week but has no fever or breast pain. She has no chronic medical conditions and does not take any medications. Breast examination shows no palpable masses or skin changes. A thin, blood-tinged discharge can be expressed from the right nipple. There are no enlarged axillary lymph nodes. Which of the following is the most likely histopathologic finding in this patient's right breast?

- ☐ A. Atypical cells infiltrating the nipple skin
- ☐ B. Cysts lined by metaplastic apocrine cells
- ☐ C. Epithelial cells lining fibrovascular cores
- ☐ D. Necrotic adipocytes with inflammation
- ☐ E. Stromal proliferation compressing the ducts to slits

Submit








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- ☐ A. Atypical cells infiltrating the nipple skin (12%)
- ☐ B. Cysts lined by metaplastic apocrine cells (10%)
- ☒ C. Epithelial cells lining fibrovascular cores (48%)
- ☐ D. Necrotic adipocytes with inflammation (7%)
- ☐ E. Stromal proliferation compressing the ducts to slits (21%)

Correct

 48%  
Answered correctly

01 min, 52 secs

Time Spent



02/04/2021

Last Updated

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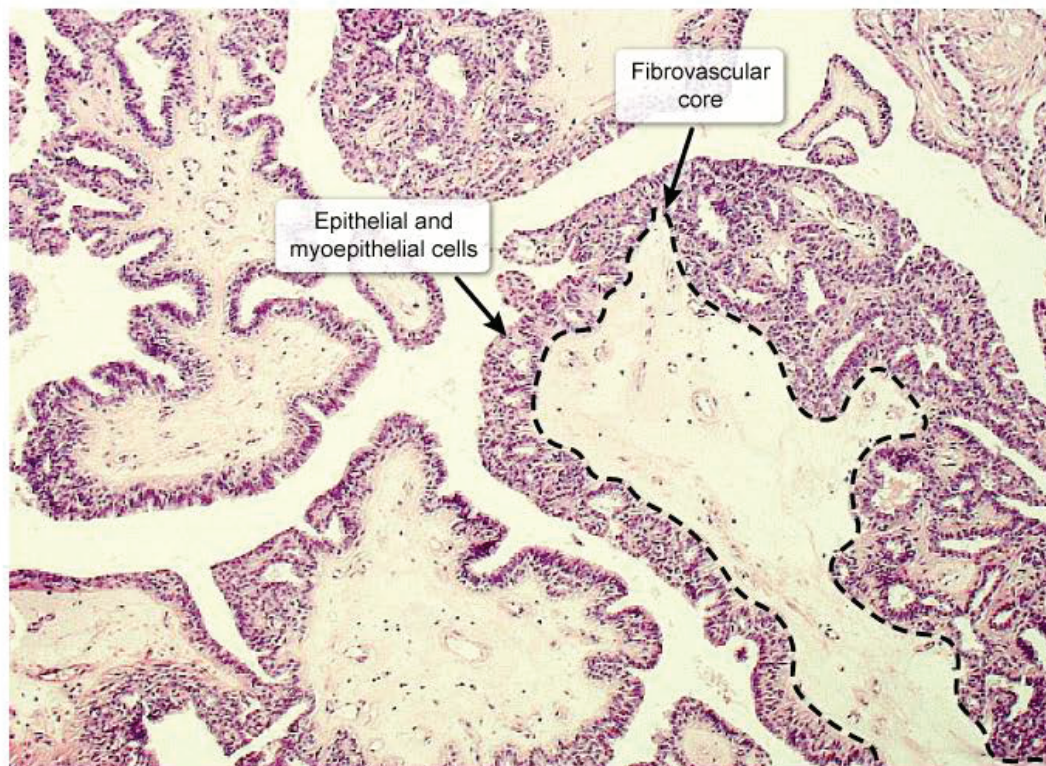
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### Intraductal papilloma







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Papillary architecture: fibrovascular core lined by epithelial cells

**Nipple discharge** can be physiologic (ie, bilateral, nonbloody or milky, without masses or skin changes) or pathologic (ie, **bloody** or serosanguineous and **unilateral** with or without palpable masses and skin changes).

The most common cause of pathologic nipple discharge is an **intraductal papilloma**, which classically presents as a unilateral, bloody nipple discharge with no associated breast masses, skin changes, or axillary lymphadenopathy. Although most cases of intraductal papilloma are benign, all patients with pathologic nipple discharge require evaluation with imaging (eg, mammogram or ultrasound, depending upon age) and possibly with biopsy. On microscopy, intraductal papilloma shows **epithelial and myoepithelial cells lining fibrovascular cores** forming papillae within a duct or cyst wall. The bloody discharge results from twisting of the vascular stalk of the papilloma in the duct.

**(Choice A)** [Paget disease of the breast](#) occurs due to the ductal spread of atypical malignant cells to the nipple epidermis. Although patients may have bloody nipple discharge, they also have a unilateral erythematous, intensely pruritic, ulcerative lesion over the nipple and areola, which is not seen in this patient.

**(Choice B)** [Fibrocystic changes of the breast](#) may show cysts with or without metaplasia and areas of

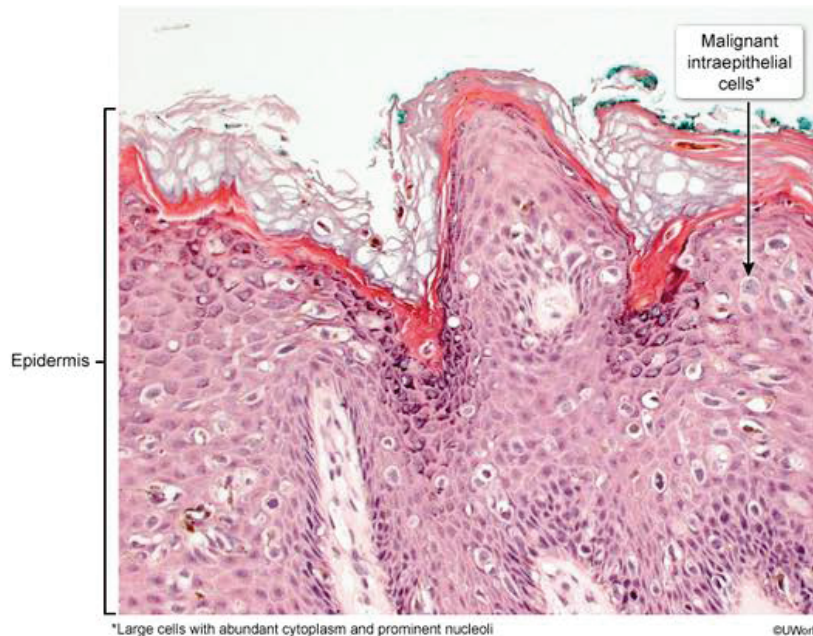






Papillary architecture: fibrovascular core lined by epithelial cells  
Exhibit Display

Paget disease of the breast



Zoom In

Zoom Out

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My Notebook



patient.

**(Choice B)** [Fibrocystic changes of the breast](#) may show cysts with or without metaplasia and areas of fibrosis. Patients with fibrocystic changes typically have cyclic breast pain, not nipple discharge.

**(Choice D)** [Fat necrosis](#) typically presents as an irregular breast mass with no associated nipple discharge after localized trauma or biopsy. Microscopy may show adipocytes undergoing necrosis with inflammation, including macrophages and giant cells.

**(Choice E)** [Fibroadenomas](#) are small, firm, and mobile breast masses that occur due to proliferation of breast stroma and ducts. Fibroadenomas do not typically cause bloody nipple discharge. Microscopic examination shows stromal proliferation compressing the ducts to slits.

### Educational objective:

Intraductal papilloma is characterized by epithelial and myoepithelial cells lining fibrovascular cores in a cyst wall or duct. It is the most common cause of bloody nipple discharge and typically presents without breast masses or skin changes.

### References

- [Common breast problems.](#)

## Exhibit Display

## Fibrocystic changes



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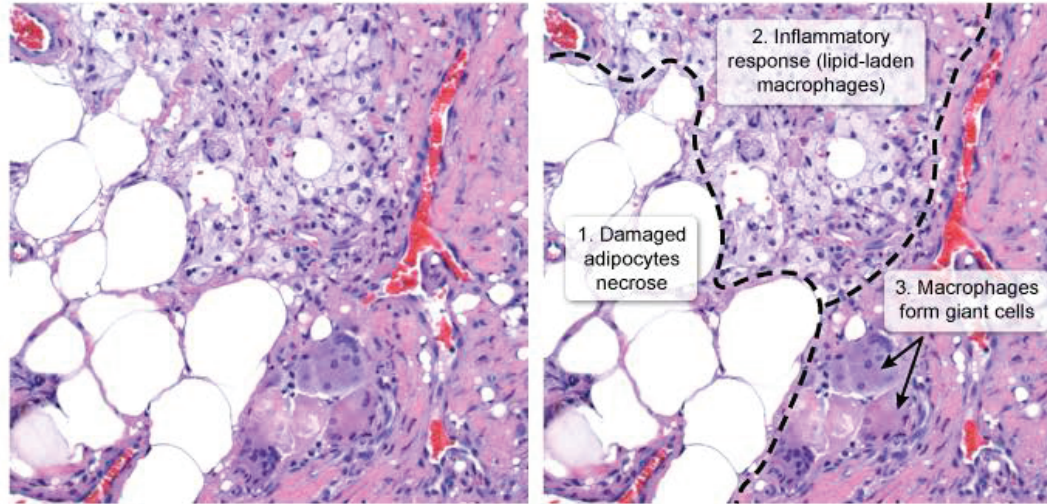
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## Exhibit Display

## Fat necrosis



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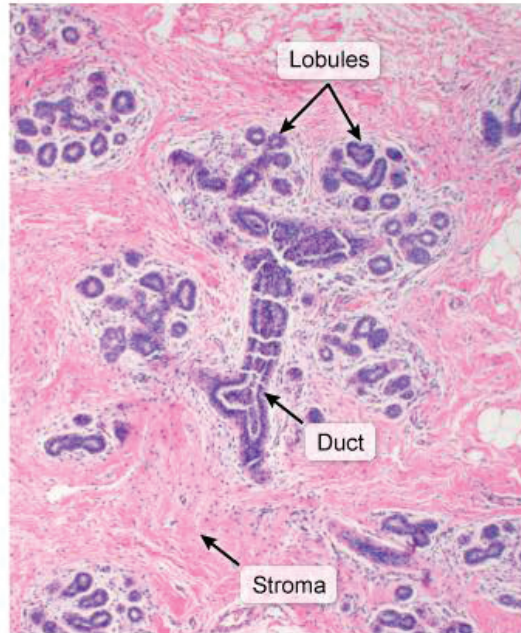
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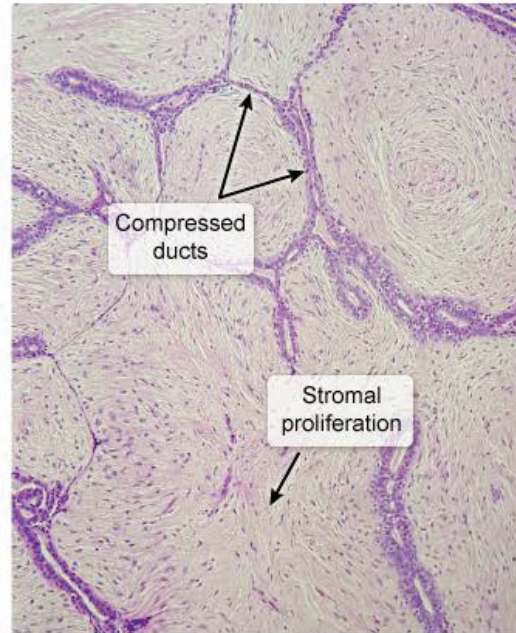
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## Exhibit Display

## Normal breast tissue



## Fibroadenoma



Zoom In

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A 49-year-old woman comes to the office for evaluation of abnormal uterine bleeding. The patient has had irregular menses for the past 2 years, but now she has been bleeding daily for 2 weeks. She also has had increased abdominal bloating and pressure but no constipation or diarrhea. Medical history includes early-stage breast cancer diagnosed at age 45 and managed with tamoxifen for the past 4 years. On examination, there is a midline, immobile pelvic mass at the level of the umbilicus. The patient undergoes hysterectomy with bilateral salpingo-oophorectomy. The final pathology report notes nuclear atypia and numerous mitoses in the affected portion of the myometrium. Which of the following is the most likely diagnosis?

- ☐ A. Adenomyosis
- ☐ B. Cervical cancer
- ☐ C. Endometritis
- ☐ D. Uterine fibroid
- ☐ E. Uterine sarcoma







irregular menses for the past 2 years, but now she has been bleeding daily for 2 weeks. She also has had increased abdominal bloating and pressure but no constipation or diarrhea. Medical history includes early-stage breast cancer diagnosed at age 45 and managed with tamoxifen for the past 4 years. On examination, there is a midline, immobile pelvic mass at the level of the umbilicus. The patient undergoes hysterectomy with bilateral salpingo-oophorectomy. The final pathology report notes nuclear atypia and numerous mitoses in the affected portion of the myometrium. Which of the following is the most likely diagnosis?

- ☐ A. Adenomyosis (15%)
- ☐ B. Cervical cancer (8%)
- ☐ C. Endometritis (4%)
- ☐ D. Uterine fibroid (9%)
- ☒ E. Uterine sarcoma (62%)

Correct

62%  
Answered correctly58 secs  
Time spent01/09/2021  
Last updated

Block Time Remaining: 00:16:46

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### Uterine sarcoma

#### Risk factors

- Tamoxifen use
- Pelvic radiation
- Postmenopausal status

#### Clinical features

- Abnormal/postmenopausal bleeding
- Bulk symptoms (eg, pelvic pressure, bloating)
- Uterine mass

#### Histopathology

- Arises from uterine smooth muscle or endometrial stromal cells
- Malignant features:
  - Cellular atypia
  - Abundant mitoses



## Histopathology • Malignant features.

- Cellular atypia
- Abundant mitoses
- Tumor cell necrosis

This patient with abnormal uterine bleeding and bulk symptoms (eg, bloating, pelvic pressure) had a midline pelvic mass similar to that caused by uterine leiomyomas (ie, fibroids). However, uterine fibroids tend to regress rather than enlarge as patients approach menopause (median age 51). In this patient, who was increasingly symptomatic and at increased risk due to **tamoxifen use**, the most concerning potential diagnosis is **uterine sarcoma**, a rare but **aggressive malignant tumor** arising from the **uterine myometrium** or endometrial connective tissue.

Because uterine sarcomas and leiomyomas often have overlapping clinical presentations and imaging findings, microscopic evaluation is required to differentiate between the two:

- Leiomyomas (uterine fibroids) are benign tumors of the uterine myometrium caused by monoclonal proliferation of myocytes and fibroblasts. Therefore, microscopy shows no nuclear atypia and a minimal number of mitotic figures (**Choice D**).
- In contrast, uterine sarcomas are rapidly progressive malignant tumors. Therefore, microscopy shows





- Leiomyomas (uterine fibroids) are benign tumors of the uterine myometrium caused by monoclonal proliferation of myocytes and fibroblasts. Therefore, microscopy shows no nuclear atypia and a minimal number of mitotic figures (**Choice D**).
- In contrast, uterine sarcomas are rapidly progressive malignant tumors. Therefore, microscopy shows myocytes and/or endometrial stromal cells with **nuclear atypia**, **abundant mitoses**, and areas of necrosis.

Treatment for uterine sarcoma is hysterectomy followed in some cases with chemotherapy and/or pelvic radiation.

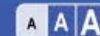
**(Choice A)** Adenomyosis, the invagination of endometrial tissue into the myometrium, commonly presents with heavy menstrual bleeding and an enlarged uterus due to increased endometrial surface area.

However, microscopy typically reveals endometrial glands embedded in the myometrium.

**(Choice B)** Cervical cancer classically presents with abnormal vaginal bleeding (eg, postcoital bleeding). Although cervical cancer can cause nuclear atypia with numerous mitoses, these abnormal changes occur in cervical squamocolumnar epithelial cells, not the myometrium.

**(Choice C)** Chronic endometritis may present with abnormal uterine bleeding; however, it does not cause





Although cervical cancer can cause nuclear atypia with numerous mitoses, these abnormal changes occur in cervical squamocolumnar epithelial cells, not the myometrium.

**(Choice C)** Chronic endometritis may present with abnormal uterine bleeding; however, it does not cause a large or immobile pelvic mass. Microscopy typically shows plasma cells within the endometrial stroma, not the myometrium.

### Educational objective:

Uterine sarcoma is a rare but aggressive malignant tumor of the uterine myometrium and/or endometrial stromal tissue. Patients typically have clinical features similar to those with uterine leiomyomas (eg, abnormal uterine bleeding, immobile pelvic mass), but uterine sarcoma can be distinguished by microscopy, which typically shows characteristic malignant features such as nuclear atypia, abundant mitoses, and tumor necrosis.

### References

- [Uterine leiomyosarcoma: a review of recent advances in molecular biology, clinical management and outcome.](#)

Pathology

Female Reproductive System &amp; Breast

Uterine fibroids

Subject

System

Topic

Block Time Remaining: 00:16:46

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Feedback



Suspend



End Block



The following vignette applies to the next **2** items. The items in the set must be answered in sequential order. Once you click **Proceed to Next Item**, you will not be able to add or change an answer.

A 24-year-old woman comes to the office for an infertility evaluation. She has had irregular menstrual cycles for the past 5 years, with menstrual periods every 2-3 months on average. Her past medical history is notable for an appendectomy 5 years ago but is otherwise not significant. The patient takes no medications. Her blood pressure is 125/86 mm Hg and pulse is 72/min. BMI is 33 kg/m<sup>2</sup>. Physical examination shows facial acne and excessive hair growth on the upper lip and chin.

### Item 1 of 2

Which of the following is the most likely pathologic finding in this patient?

- ☐ A. Atrophic endometrium
- ☐ B. Bilateral adrenal atrophy
- ☐ C. Enlarged ovaries
- ☐ D. Pituitary adenoma







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### Item 1 of 2

Which of the following is the most likely pathologic finding in this patient?

- ☐ A. Atrophic endometrium
- ☐ B. Bilateral adrenal atrophy
- ☐ C. Enlarged ovaries
- ☐ D. Pituitary adenoma
- ☐ E. Polycystic kidneys

Submit





A 24-year-old woman comes to the office for an infertility evaluation. She has had irregular menstrual cycles for the past 5 years, with menstrual periods every 2-3 months on average. Her past medical history is notable for an appendectomy 5 years ago but is otherwise not significant. The patient takes no medications. Her blood pressure is 125/86 mm Hg and pulse is 72/min. BMI is 33 kg/m<sup>2</sup>. Physical examination shows facial acne and excessive hair growth on the upper lip and chin.

### Item 1 of 2

Which of the following is the most likely pathologic finding in this patient?

- ☐ A. Atrophic endometrium (4%)
- ☐ B. Bilateral adrenal atrophy (1%)
- ☒ C. Enlarged ovaries (77%)
- ☐ D. Pituitary adenoma (4%)
- ☐ E. Polycystic kidneys (12%)

Correct

77%

29 secs

01/16/2021

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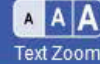
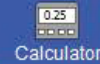
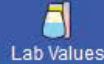
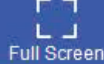
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End Block



Polycystic ovary syndrome	
Clinical features	<ul style="list-style-type: none"><li>• <b>Androgen excess:</b> Hirsutism, acne, androgenic alopecia</li><li>• <b>Ovarian dysfunction:</b> Menstrual irregularity, polycystic ovaries</li><li>• <b>Insulin resistance:</b> Acanthosis nigricans, glucose intolerance/diabetes, metabolic syndrome</li><li>• <b>Obesity</b></li></ul>
Treatment	<ul style="list-style-type: none"><li>• Weight loss</li><li>• Combination hormonal contraceptives</li><li>• Metformin (if hyperglycemia/diabetes)</li></ul>

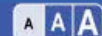
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This patient with obesity, menstrual irregularities, and hirsutism most likely has **polycystic ovary syndrome** (PCOS). The etiology of PCOS is heterogeneous and multifactorial and involves both genetic and environmental factors (eg, diet, obesity).

PCOS is characterized by a number of hormonal abnormalities that may be present to varying degrees. LH levels are typically elevated, and patients may also have increased LH activity at the ovary (increased LH receptor expression). Most patients also have insulin resistance and elevated insulin levels, often with







PCOS is characterized by a number of hormonal abnormalities that may be present to varying degrees. LH levels are typically elevated, and patients may also have increased LH activity at the ovary (increased LH receptor expression). Most patients also have insulin resistance and elevated insulin levels, often with obesity, dyslipidemia, and an increased risk of diabetes and cardiovascular disease. PCOS is also characterized by increased ovarian and/or adrenal **androgen production**, likely due to the effects of LH, insulin, and possibly additional genetic factors. In addition to systemic manifestations (eg, acne, hirsutism, male-pattern hair loss), excess androgen levels in the ovaries cause anovulation/infertility, oligomenorrhea, and enlarged ovaries with multiple cysts.

**(Choice A)** Estrogen levels are also elevated chronically in patients with PCOS. This may cause endometrial hyperplasia and possibly an increased risk of endometrial carcinoma.

**(Choices B and D)** Cushing syndrome (CS) is caused by cortisol excess, usually due to a hyperfunctioning adrenal adenoma or an ACTH-producing pituitary adenoma. CS and PCOS share several clinical features, such as obesity, hirsutism, and menstrual irregularities. However, patients with CS typically also have moon facies, enlarged supraclavicular and dorsocervical fat pads, skin atrophy, and proximal muscle weakness. CS due to an adrenal adenoma may cause contralateral adrenal atrophy but not bilateral atrophy.

**(Choice E)** Polycystic kidney disease is an inherited condition with juvenile and adult forms. Patients



**(Choices B and D)** Cushing syndrome (CS) is caused by cortisol excess, usually due to a hyperfunctioning adrenal adenoma or an ACTH-producing pituitary adenoma. CS and PCOS share several clinical features, such as obesity, hirsutism, and menstrual irregularities. However, patients with CS typically also have moon facies, enlarged supraclavicular and dorsocervical fat pads, skin atrophy, and proximal muscle weakness. CS due to an adrenal adenoma may cause contralateral adrenal atrophy but not bilateral atrophy.

**(Choice E)** Polycystic kidney disease is an inherited condition with juvenile and adult forms. Patients typically have hypertension, flank pain, recurrent urinary tract infections, hematuria, and renal insufficiency.

### Educational objective:

Polycystic ovary syndrome is characterized by elevated LH levels, excess androgen production, and insulin resistance. Clinical features include obesity, menstrual irregularities, hirsutism, enlarged ovaries, and an increased risk of diabetes mellitus and endometrial hyperplasia.

### References

- [Polycystic ovarian syndrome.](#)

Pathophysiology	Female Reproductive System & Breast	Polycystic ovary disease
Subject	System	Topic



## Item 2 of 2

The patient wishes to discuss treatment options. Which of the following treatment mechanisms best addresses her infertility problem?

- ☐ A. 11-beta-hydroxylase antagonism
- ☐ B. Androgen receptor antagonism
- ☐ C. Dopamine receptor agonism
- ☐ D. Estrogen receptor modulation
- ☐ E. Progesterone supplementation

Submit







## Item 2 of 2

The patient wishes to discuss treatment options. Which of the following treatment mechanisms best addresses her infertility problem?

- ☐ A. 11-beta-hydroxylase antagonism (1%)
- ☐ B. Androgen receptor antagonism (31%)
- ☐ C. Dopamine receptor agonism (1%)
- ☒ D. Estrogen receptor modulation (43%)
- ☐ E. Progesterone supplementation (22%)

Correct



43%

Answered correctly



30 secs

Time Spent



01/16/2021

Last Updated

Explanation





Patients who are obese and have polycystic ovary syndrome (PCOS) should be advised on **weight loss**, which can often reverse insulin resistance and restore normal ovulatory function. Those who do not wish to become pregnant may also be started on dual estrogen-progestin **oral contraceptive pills** to minimize endometrial proliferation, reduce androgenic symptoms (eg, hirsutism, acne), and prevent unwanted pregnancy.

For those who do wish to become pregnant, if weight loss does not restore ovulation, medications aimed at inducing ovulation (eg, clomiphene, letrozole) are used. **Clomiphene** is a selective estrogen receptor modulator that prevents negative feedback inhibition on the hypothalamus and pituitary by circulating estrogen, resulting in increased gonadotropin production (FSH and LH) and ovulation.

**(Choice A)** Metyrapone, an 11-beta-hydroxylase inhibitor, blocks synthesis of cortisol. The resulting increase in pituitary ACTH release leads to increased adrenal androgen production and would worsen androgenic symptoms.

**(Choice B)** Spironolactone is an androgen receptor antagonist used in the treatment of acne and hirsutism for PCOS patients who do not respond adequately to oral contraceptive pills. It is not used in those who wish to become pregnant due to the risk of fetal abnormalities.





**(Choice B)** Spironolactone is an androgen receptor antagonist used in the treatment of acne and hirsutism for PCOS patients who do not respond adequately to oral contraceptive pills. It is not used in those who wish to become pregnant due to the risk of fetal abnormalities.

**(Choice C)** Dopamine agonists (eg, bromocriptine, cabergoline) decrease pituitary release of prolactin and are useful in patients with infertility due to hyperprolactinemia. They are not useful in PCOS.

**(Choice E)** Progestin-only medications directly inhibit the endometrium and can be used to minimize endometrial hyperplasia in patients with PCOS. However, these medications would not enhance fertility and, unlike dual estrogen-progestin medications, would not improve hirsutism and acne.

### Educational objective:

Patients with polycystic ovary syndrome who desire fertility can be treated with clomiphene. Clomiphene is an estrogen receptor modulator that decreases negative feedback inhibition on the hypothalamus by circulating estrogen, thereby increasing gonadotropin production.

### References

- [The treatment of infertility in polycystic ovary syndrome: a brief update.](#)

Pathophysiology

Female Reproductive System &amp; Breast

Polycystic ovary disease







A 23-year-old woman is being evaluated for recurrent episodes of urinary tract infection. She has had 5 episodes of cystitis and an episode of pyelonephritis over the past year. The symptoms tend to occur a few days following sexual intercourse. The patient has no other medical problems and takes no medications. Her temperature is 36.7 C (98 F), blood pressure is 110/70 mm Hg, respirations are 16/min, and pulse is 65/min. Abdominal and genitourinary examinations are normal. Which of the following is the most likely predisposing factor for pyelonephritis in this patient?

- ☐ A. Frequent voiding
- ☐ B. Hematogenous bacterial spread
- ☐ C. Suppression of endogenous flora
- ☐ D. Urethral colonization
- ☐ E. Vesicoureteral urine reflux

**Submit**



A 23-year-old woman is being evaluated for recurrent episodes of urinary tract infection. She has had 5 episodes of cystitis and an episode of pyelonephritis over the past year. The symptoms tend to occur a few days following sexual intercourse. The patient has no other medical problems and takes no medications. Her temperature is 36.7 C (98 F), blood pressure is 110/70 mm Hg, respirations are 16/min, and pulse is 65/min. Abdominal and genitourinary examinations are normal. Which of the following is the most likely predisposing factor for pyelonephritis in this patient?

- ☐ A. Frequent voiding (0%)
- ☐ B. Hematogenous bacterial spread (1%)
- ☐ C. Suppression of endogenous flora (4%)
- ☒ D. Urethral colonization (31%)
- ☐ E. Vesicoureteral urine reflux (61%)

**Incorrect**

Correct answer

E



61%

Answered correctly



59 secs

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The bacteria that usually cause **urinary tract infections (UTIs)** such as cystitis (bladder infection) and pyelonephritis (kidney infection) typically originate from fecal flora and include gram-negative rods (eg, *Escherichia coli*, *Klebsiella*, *Proteus*) and *Enterococcus*. In women, sexual intercourse facilitates bacterial ascent up the relatively **short urethra** and into the bladder, which has several antibacterial defenses, including:

- The bladder mucosa normally does not allow bacterial attachment
- Normal urine is bactericidal due to high urea content and osmolarity
- **Urine flow** washes the bacteria downstream

When these mechanisms are disrupted or overcome due to bacterial **virulence factors** (eg, fimbriae to facilitate attachment, capsule to resist phagocytosis), **cystitis** occurs.

The normal vesicoureteral junction does not allow retrograde flow of urine. If there is an anatomic abnormality of this area or an increase in bladder pressure, some urine returns to the ureter, carrying any pathogens present in the bladder (**vesicoureteral reflux**). Frequent bladder infections, such as in this patient, may weaken the vesicoureteral junction and facilitate reflux. Without vesicoureteral reflux, the ascent of pathogens to the kidneys is very unlikely, and **pyelonephritis** does not occur.

**(Choice A)** Frequent voiding may be a symptom of UTI but does not cause the infection. In fact, frequent





**(Choice A)** Frequent voiding may be a symptom of UTI but does not cause the infection. In fact, frequent urination may prevent UTIs by washing pathogens away. Frequency of sexual intercourse is an important risk factor for recurrent UTIs.

**(Choice B)** Hematogenous bacterial spread is a possible cause of acute pyelonephritis. This mechanism is most significant in hospitalized, elderly, debilitated patients with multiple potential infectious sources or significantly weakened immune defenses. This patient is young and generally healthy with no signs of systemic infection or immunosuppression, making hematogenous spread very unlikely.

**(Choices C and D)** Normal urethral flora microorganisms (lactobacilli, nonpathogenic staphylococci and streptococci) do not multiply readily in urine and generally do not cause infection. Suppression of this endogenous flora can occur in pregnancy, with antibiotic use, or during a systemic illness and may facilitate distal urethral colonization by pathogenic gram-negative rods. This may play an important role in the development of lower UTIs but generally is not sufficient to cause pyelonephritis.

**Educational objective:**

Suppression of endogenous flora, colonization of the distal urethra by pathogenic gram-negative rods, and attachment of these pathogens to the bladder mucosa are the stages of pathogenesis in lower urinary tract infections. Anatomic or functional vesicoureteral reflux is almost always necessary for the development of acute pyelonephritis.



A 28-year-old woman, gravida 1, para 0, goes into labor at 38 weeks gestation. During the second stage, as the patient is pushing, the fetus develops a nonreassuring fetal heart rate. A midline episiotomy is performed to expedite delivery. A vertical, midline incision is made at the posterior vaginal opening through the vaginal and subvaginal mucosa. Which of the following structures is most likely involved in this incision?

- ☐ A. External anal sphincter
- ☐ B. Ischiocavernosus muscle
- ☐ C. Levator ani muscle
- ☐ D. Perineal body
- ☐ E. Rectal mucosa
- ☐ F. Transverse perineal muscle

Submit





A 28-year-old woman, gravida 1, para 0, goes into labor at 38 weeks gestation. During the second stage, as the patient is pushing, the fetus develops a nonreassuring fetal heart rate. A midline episiotomy is performed to expedite delivery. A vertical, midline incision is made at the posterior vaginal opening through the vaginal and subvaginal mucosa. Which of the following structures is most likely involved in this incision?

- ☐ A. External anal sphincter (7%)
- ☐ B. Ischiocavernosus muscle (5%)
- ☐ C. Levator ani muscle (17%)
- ☒ D. Perineal body (48%)
- ☐ E. Rectal mucosa (2%)
- ☐ F. Transverse perineal muscle (17%)

Correct



48%

Answered correctly



48 secs

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01/22/2021

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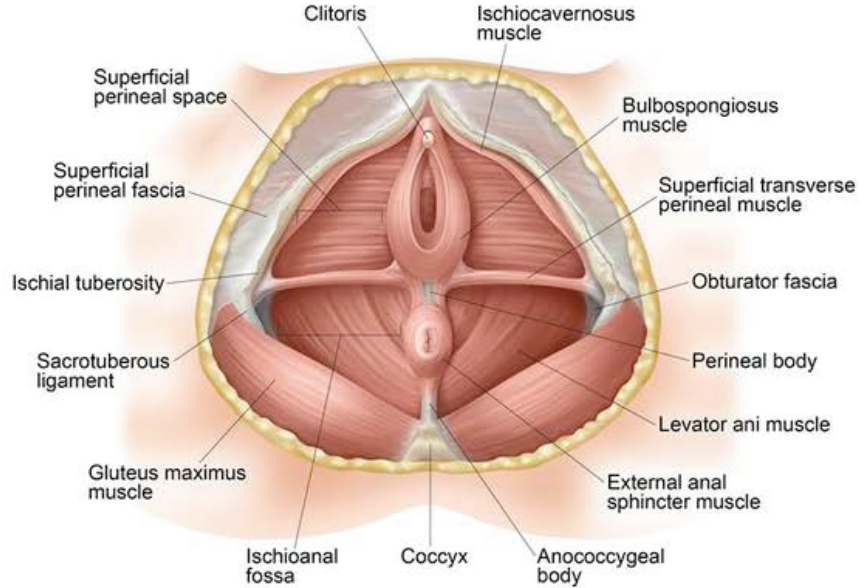


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### Exhibit Display

#### Pelvic floor muscles



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The **perineal body** is essential to the integrity of the pelvic floor. This **tendinous center point of the perineum** separates the urogenital and anal triangles. It blends anteriorly with the perineal membrane and superiorly with the rectovesical or rectovaginal septum. The following structures are anchored to the perineal body:

- Bulbospongiosus muscle
- External anal sphincter muscle
- Superficial and deep transverse perineal muscles
- Fibers from the external urethral sphincter, levator ani, and muscular coat of the rectum

Episiotomies are used to enlarge the vaginal outlet to facilitate delivery and reduce the risk of severe perineal laceration. A **midline episiotomy** is a vertical incision from the posterior vaginal opening to the perineal body. It transects the vaginal lining and the submucosal tissue but not the external anal sphincter or the rectal mucosa (**Choice E**). Improper repair of a midline episiotomy may result in pelvic organ prolapse or dyspareunia.

**(Choice A)** The external anal sphincter is part of the anal triangle. It arises from the coccyx and anococcygeal ligament and inserts into the perineal body. Women with severe perineal lacerations are at risk for fecal incontinence due to anal sphincter damage.





**(Choice A)** The external anal sphincter is part of the anal triangle. It arises from the coccyx and anococcygeal ligament and inserts into the perineal body. Women with severe perineal lacerations are at risk for fecal incontinence due to anal sphincter damage.

**(Choice B)** The ischiocavernosus muscle is part of the urogenital triangle. It arises from the inner surface of the ischial tuberosities and the ischiopubic rami and inserts into the corpus cavernosum. When the clitoris is stimulated, the ischiocavernosus muscle forces blood into the clitoris.

**(Choice C)** The levator ani muscle (part of the anal triangle) supports the pelvic floor and can be strengthened by Kegel exercises. This muscle is often stretched, pushed aside, and torn by fetal crowning and delivery. It is not usually incised during an episiotomy.

**(Choice F)** The transverse perineal muscle is part of the superficial perineal space (urogenital triangle). It arises from the ischial rami and tuberosities and inserts into the perineal body. This muscle is cut during a mediolateral episiotomy.

### **Educational objective:**

The perineal body is a fibromuscular tissue between the urogenital and anal triangle. A midline episiotomy is a vertical incision from the posterior vaginal opening to the perineal body. It transects the vaginal submucosal tissue but not the external anal sphincter or the rectal mucosa.







A 63-year-old woman comes to the office for evaluation of chronic constipation. For the past 8 months, the patient has had increased straining with bowel movements but no abdominal pain or rectal bleeding. She has 2 children, both delivered via forceps-assisted vaginal delivery. BMI is 31 kg/m<sup>2</sup>. On digital rectal examination, there are no masses and rectal tone is normal; pelvic examination shows a visible bulge into the vagina with straining. Sensation around the perineum is intact. Fecal occult blood testing is negative. Which of the following is the most likely cause of this patient's symptoms?

- ☐ A. Absence of colonic intramural ganglion cells
- ☐ B. Colonic sensitivity with chronic irregular contractions
- ☐ C. Damage to the levator ani muscle complex
- ☐ D. Defect in the external anal sphincter
- ☐ E. Increased internal anal sphincter parasympathetic tone

Submit






A 63-year-old woman comes to the office for evaluation of chronic constipation. For the past 8 months, the patient has had increased straining with bowel movements but no abdominal pain or rectal bleeding. She has 2 children, both delivered via forceps-assisted vaginal delivery. BMI is 31 kg/m<sup>2</sup>. On digital rectal examination, there are no masses and rectal tone is normal; pelvic examination shows a visible bulge into the vagina with straining. Sensation around the perineum is intact. Fecal occult blood testing is negative. Which of the following is the most likely cause of this patient's symptoms?

- ☐ A. Absence of colonic intramural ganglion cells (2%)
- ☐ B. Colonic sensitivity with chronic irregular contractions (3%)
- ☒ C. Damage to the levator ani muscle complex (78%)
- ☐ D. Defect in the external anal sphincter (7%)
- ☐ E. Increased internal anal sphincter parasympathetic tone (7%)

Correct

 78%  
Answered correctly

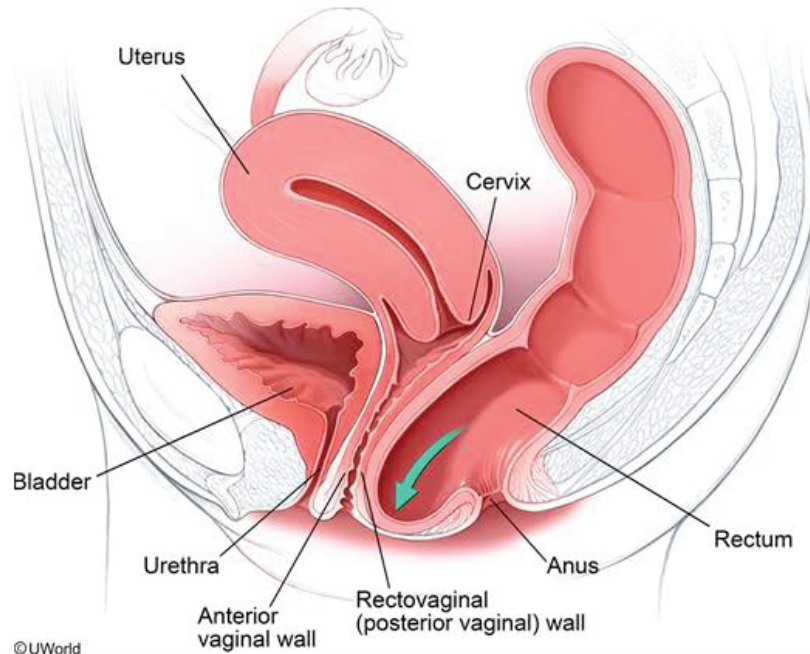
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Exhibit Display

Rectocele, prolapse of posterior vaginal wall



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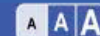
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This patient's chronic constipation is caused by **pelvic organ prolapse**, the herniation of pelvic organs (eg, bladder, rectum) into the vaginal wall due to **levator ani muscle complex damage**. The levator ani muscle complex forms most of the pelvic floor and functions to hold the pelvic organs in a stable position; when this complex is damaged, such as with increased intraabdominal pressure (eg, **pregnancy**, obesity) or obstetric trauma (eg, forceps-assisted vaginal delivery), there is increased pelvic floor laxity, resulting in decreased pelvic organ support.

The decreased pelvic floor support causes an anatomic change to normal pelvic organ positions; for the rectum, this leads to a change in rectal angle during defecation, which can cause incomplete defecation and **constipation**. With accumulation of fecal material, the rectum expands and herniates through the rectovaginal septum, causing **prolapse of the rectum** into the **posterior vaginal wall** (ie, **rectocele**). The prolapse is exacerbated by Valsalva maneuvers (eg, **vaginal bulge while straining**), which cause further difficulty with defecation; therefore, some patients apply digital pressure against the prolapse (ie, **splinting**) to help improve bowel movements.

**(Choice A)** **Hirschsprung disease**, the absence of colonic intramural ganglion cells due to failed neural crest cell migration, typically presents in infants. It causes constipation and increased rectal tone due to the inability of the aganglionic segment to relax.





the inability of the aganglionic segment to relax.

**(Choice B)** Irritable bowel syndrome (IBS) is often associated with chronic irregular luminal contractions and increased gastrointestinal tract sensitivity. It typically presents with recurrent abdominal pain and either diarrhea or constipation. IBS does not affect the pelvic floor musculature and, therefore, does not cause a vaginal bulge.

**(Choice D)** An external anal sphincter defect occurs with a [perineal laceration](#), a common complication of vaginal deliveries; however, patients typically have decreased rectal tone (not seen here) that can result in anal incontinence (ie, involuntary loss of flatus or fecal material).

**(Choice E)** The internal anal sphincter (IAS) is under tonic contraction via sympathetic fibers; contraction is inhibited by parasympathetic fibers. Increased IAS parasympathetic tone would cause sphincter relaxation and an increased urge to defecate rather than chronic constipation.

### Educational objective:

Pelvic organ prolapse, the herniation of pelvic organs (eg, rectum) into the vagina, occurs due to damage to the levator ani muscle complex. Patients with prolapse of the posterior vaginal wall (ie, rectocele) classically have chronic constipation and a vaginal bulge.

### References





A 26-year-old woman, gravida 1, para 1, comes to the office for a routine examination. She noticed new facial hair over the past few months and thinks her voice is deeper. Her last menstrual period was 5 months ago. The patient's mother died from invasive lobular breast carcinoma at age 60. Physical examination is significant for coarse facial hair, and pelvic examination reveals clitoromegaly with a large adnexal mass. Urine pregnancy test is negative. Pelvic ultrasonography confirms a large ovarian cyst. Which of the following is the most likely diagnosis?

- ☐ A. Dysgerminoma
- ☐ B. Endodermal sinus tumor
- ☐ C. Granulosa cell tumor
- ☐ D. Mature cystic teratoma
- ☐ E. Serous cystadenocarcinoma
- ☐ F. Sertoli-Leydig tumor

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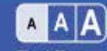


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A 26-year-old woman, gravida 1, para 1, comes to the office for a routine examination. She noticed new facial hair over the past few months and thinks her voice is deeper. Her last menstrual period was 5 months ago. The patient's mother died from invasive lobular breast carcinoma at age 60. Physical examination is significant for coarse facial hair, and pelvic examination reveals clitoromegaly with a large adnexal mass. Urine pregnancy test is negative. Pelvic ultrasonography confirms a large ovarian cyst. Which of the following is the most likely diagnosis?

- ☐ A. Dysgerminoma (6%)
- ☐ B. Endodermal sinus tumor (0%)
- ☐ C. Granulosa cell tumor (18%)
- ☐ D. Mature cystic teratoma (3%)
- ☐ E. Serous cystadenocarcinoma (6%)
- ☒ F. Sertoli-Leydig tumor (64%)





## Malignant ovarian neoplasms

Histologic type	Diagnosis	Key features
Epithelial	Serous cystadenocarcinoma	<ul style="list-style-type: none"><li>• Most common ovarian cancer</li><li>• Often bilateral</li><li>• Histology: Psammoma bodies</li></ul>
	Mucinous cystadenocarcinoma	<ul style="list-style-type: none"><li>• Pseudomyxoma peritonei</li><li>• Mucin-producing epithelial cells</li></ul>
Germ cell	Dysgerminoma	<ul style="list-style-type: none"><li>• Adolescents</li><li>• <math>\uparrow \beta\text{-hCG}</math>, <math>\uparrow \text{LDH}</math></li><li>• Histology: "Fried egg cells"</li></ul>
	Endodermal sinus (yolk sac)	<ul style="list-style-type: none"><li>• <math>\uparrow \text{AFP}</math></li><li>• Aggressive</li><li>• Schiller-Duval bodies resemble glomeruli</li></ul>
		<ul style="list-style-type: none"><li>• <math>\uparrow \text{Estrogen}</math> (eg, endometrial hyperplasia, postmenopausal bleeding)</li></ul>





	(yolk sac)	<ul style="list-style-type: none"><li>• Schiller-Duval bodies resemble glomeruli</li></ul>
Stroma (sex cord)	Granulosa cell	<ul style="list-style-type: none"><li>• ↑ Estrogen (eg, endometrial hyperplasia, postmenopausal bleeding)</li><li>• ↑ Inhibin</li><li>• Histology: Call-Exner bodies, coffee bean nuclei</li></ul>
	Sertoli-Leydig	<ul style="list-style-type: none"><li>• ↑ Androgens (eg, hirsutism, clitoromegaly)</li></ul>

**AFP** = alpha-fetoprotein; **LDH** = lactate dehydrogenase.

A **Sertoli-Leydig cell ovarian tumor** typically presents as a large adnexal mass with amenorrhea and **virilization** (eg, hirsutism, clitoromegaly, deeper voice). Virilization occurs due to increased testosterone secretion by this rare **sex cord-stromal** tumor. Patients with this neoplasm are usually young women, and it is histopathologically similar to Sertoli cell testicular neoplasms. Microscopic examination of these tumors shows hollow or solid tubules lined by round Sertoli cells and surrounded by a fibrous stroma.

**(Choice A)** A dysgerminoma is a malignant germ cell ovarian tumor that does not secrete testosterone and typically presents as a rapidly growing mass or a ruptured ovarian cyst. It is a common cause of ovarian cancer in pregnancy. Histology shows vesicular cells with clear cytoplasm and large central nuclei







shows hollow or solid tubules lined by round Sertoli cells and surrounded by a fibrous stroma.

**(Choice A)** A dysgerminoma is a malignant germ cell ovarian tumor that does not secrete testosterone and typically presents as a rapidly growing mass or a ruptured ovarian cyst. It is a common cause of ovarian cancer in pregnancy. Histology shows vesicular cells with clear cytoplasm and large central nuclei due to an increased nucleus to cytoplasm ratio (eg, "fried egg cells").

**(Choice B)** An endodermal sinus (eg, yolk sac) tumor is a malignant germ cell ovarian tumor that typically presents with abdominal pain due to ovarian torsion without virilization. The neoplasm is characterized by **Schiller-Duval bodies**, which are glomerulus-like papillary structures with a central vessel (black arrow).

**(Choice C)** A granulosa cell tumor is a rare sex cord-stromal tumor that produces excessive estrogen (eg, abnormal uterine bleeding due to endometrial hyperplasia, precocious puberty). These tumors are characterized by Call-Exner bodies, small follicle-like structures filled with eosinophilic secretions that are lined by granulosa cells containing **coffee bean nuclei** (black arrows).

**(Choice D)** A mature cystic teratoma, the most common benign germ cell tumor, is usually identified as a nonfunctional adnexal mass in an asymptomatic patient. Pathologic findings include keratinized epithelial tissue with **sebaceous glands**.

**(Choice E)** Serous cystadenocarcinoma is the most common epithelial ovarian cancer that classically





Item 23 of 40

Question Id: 1928



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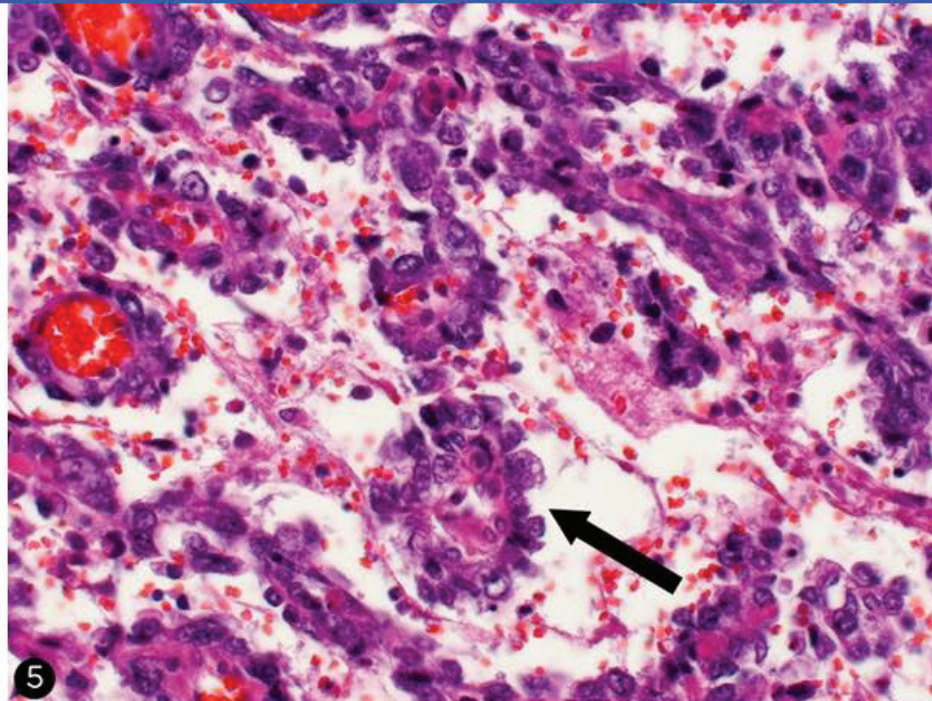


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(Choice 5) Serous cystadenocarcinoma is the most common epithelial ovarian cancer that classically

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Item 23 of 40

Question Id: 1928



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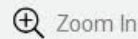


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(Choice E) Serous cystadenocarcinoma is the most common epithelial ovarian cancer that classically

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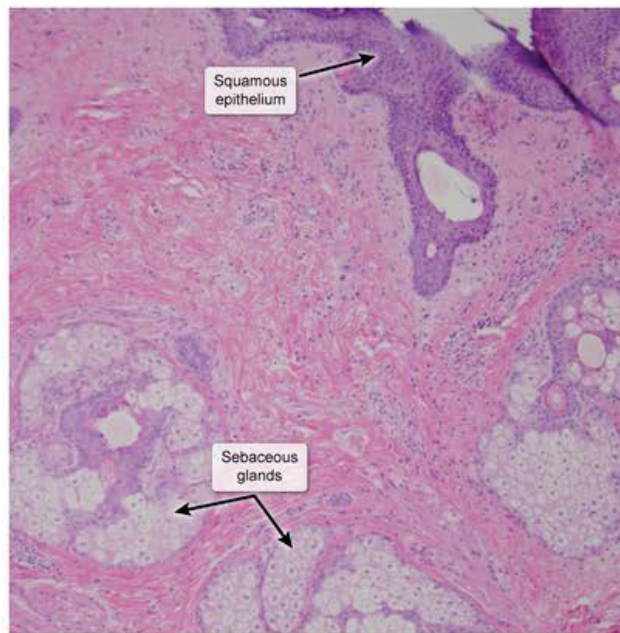
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## Exhibit Display

## Mature teratoma of the ovary



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lined by granulosa cells containing coffee bean nuclei (black arrows).

**(Choice D)** A mature cystic teratoma, the most common benign germ cell tumor, is usually identified as a nonfunctional adnexal mass in an asymptomatic patient. Pathologic findings include keratinized epithelial tissue with sebaceous glands.

**(Choice E)** Serous cystadenocarcinoma is the most common epithelial ovarian cancer that classically presents in a post-menopausal patient who has an adnexal mass and ascites without excess hormonal activity. Psammoma bodies are concentrically laminated, calcified spheric deposits found on biopsy.

### Educational objective:

Sertoli-Leydig cell tumors of the ovary arise from the sex cord stroma and secrete testosterone. Typical features include a large ovarian mass and signs of virilization. Tubular structures lined by round Sertoli cells and surrounded by a fibrous stroma are seen on pathology.

### References

- Granulosa cell tumor of the ovary: tumor review.
- Sertoli-Leydig cell tumor with heterologous element: a case report and a review of the literature.

Pathology Female Reproductive System & Breast Ovarian cancer

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A 20-year-old woman comes to the office due to 6 hours of right lower quadrant pain. The pain came on suddenly and has become intense and constant. She has been unable to eat or drink today due to nausea and frequent vomiting. The patient has had 2 sexual partners in the last year and has a history of chlamydial cervicitis. She takes ibuprofen for dysmenorrhea on the first day of her menses. The patient has a 6-cm, right ovarian cyst, which was noted on ultrasound last year. Her last menstrual period was 3 weeks ago. Temperature is 37.2 C (99 F), blood pressure is 110/80 mm Hg, and pulse is 104/min. Abdominal examination shows tenderness to deep palpation in the right lower quadrant. Urine pregnancy test is negative. Leukocyte count is 8,000/mm<sup>3</sup>. Which of the following is the most likely diagnosis?

- ☐ A. Acute appendicitis
- ☐ B. Ectopic pregnancy
- ☐ C. Endometriosis
- ☐ D. Ovarian torsion
- ☐ E. Tuboovarian abscess







suddenly and has become intense and constant. She has been unable to eat or drink today due to nausea and frequent vomiting. The patient has had 2 sexual partners in the last year and has a history of chlamydial cervicitis. She takes ibuprofen for dysmenorrhea on the first day of her menses. The patient has a 6-cm, right ovarian cyst, which was noted on ultrasound last year. Her last menstrual period was 3 weeks ago. Temperature is 37.2 C (99 F), blood pressure is 110/80 mm Hg, and pulse is 104/min. Abdominal examination shows tenderness to deep palpation in the right lower quadrant. Urine pregnancy test is negative. Leukocyte count is 8,000/mm<sup>3</sup>. Which of the following is the most likely diagnosis?

- ☐ A. Acute appendicitis (10%)
- ☐ B. Ectopic pregnancy (6%)
- ☐ C. Endometriosis (5%)
- ☒ D. Ovarian torsion (69%)
- ☐ E. Tuboovarian abscess (7%)

Correct

69%



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Ovarian torsion	
Anatomy	<ul style="list-style-type: none"><li>• Rotation of ovary around infundibulopelvic (suspensory) &amp; uteroovarian ligaments</li></ul>
Clinical features	<ul style="list-style-type: none"><li>• Sudden-onset unilateral pelvic pain</li><li>• Nausea &amp; vomiting</li><li>• ± Palpable adnexal mass</li></ul>
Ultrasound	<ul style="list-style-type: none"><li>• Doppler shows absent blood flow to ovary</li></ul>
Treatment	<ul style="list-style-type: none"><li>• Surgery for detorsion</li></ul>

This patient's presentation suggests **ovarian torsion**, a gynecologic emergency most commonly affecting reproductive-aged women. **Ovarian torsion** is the partial or complete rotation of the ovary around the infundibulopelvic (suspensory ligament of the ovary) and uteroovarian ligaments, which can affect ovarian blood supply because the ovarian vessels travel in the **infundibulopelvic ligament**. Right-sided torsion is more common because of the greater length of the right uteroovarian ligament and because the



infundibulopelvic (suspensory ligament of the ovary) and uteroovarian ligaments, which can affect ovarian blood supply because the ovarian vessels travel in the **infundibulopelvic ligament**. Right-sided torsion is more common because of the greater length of the right uteroovarian ligament and because the rectosigmoid colon takes up space around the left ovary (leaving less room for movement). Risk factors include pregnancy, ovulation induction (used for infertility treatment), and **ovarian masses  $\geq 5$  cm**.

Patients typically have **lower abdominal pain** (often sudden), nausea, and vomiting. Physical examination typically shows unilateral abdominal or **pelvic tenderness**. Peritoneal signs (rebound, involuntary guarding) and fever may develop if the ovary becomes necrotic. Initial evaluation includes complete blood count and pregnancy test (to exclude ectopic pregnancy). Leukocyte count is nonspecific because it may be normal or elevated with ovarian torsion. The diagnosis is confirmed with pelvic ultrasound showing an adnexal mass with absent Doppler flow.

**(Choices A and E)** Appendicitis and tuboovarian abscess can cause acute right lower quadrant pain; however, both diagnoses are unlikely in this afebrile patient with no leukocytosis.

**(Choice B)** Ectopic pregnancy can present with diffuse or localized abdominal pain and vaginal bleeding. A negative urine pregnancy test and menses occurring only 3 weeks earlier make ectopic pregnancy extremely unlikely.



adnexal mass with absent Doppler flow.

**(Choices A and E)** Appendicitis and tuboovarian abscess can cause acute right lower quadrant pain; however, both diagnoses are unlikely in this afebrile patient with no leukocytosis.

**(Choice B)** Ectopic pregnancy can present with diffuse or localized abdominal pain and vaginal bleeding. A negative urine pregnancy test and menses occurring only 3 weeks earlier make ectopic pregnancy extremely unlikely.

**(Choice C)** Endometriosis typically presents with chronic pelvic pain, dysmenorrhea, deep dyspareunia, and infertility. This patient's sudden onset of pain makes this diagnosis less likely.

**Educational objective:**

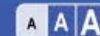
Ovarian torsion typically occurs in reproductive-aged women due to rotation of the ovary around the infundibulopelvic (suspensory) and uteroovarian ligaments. Patients typically have sudden-onset unilateral pelvic pain and a tender adnexal mass.

Pathophysiology  
Subject

Female Reproductive System & Breast  
System

Ovarian Torsion  
Topic

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A 48-year-old woman comes to the office due to painful, heavy menses for the past 6 months. The patient has 4-5 days of heavy bleeding, often soaking through a tampon or sanitary napkin every few hours. Menstrual periods occur every 28-30 days. The patient is not on contraception and has no significant medical history. Vital signs are normal. Urine pregnancy test is negative. After an appropriate workup, a hysterectomy is performed, and the surgical specimen is shown below:





Item 25 of 40

Question Id: 20237



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Lab Values



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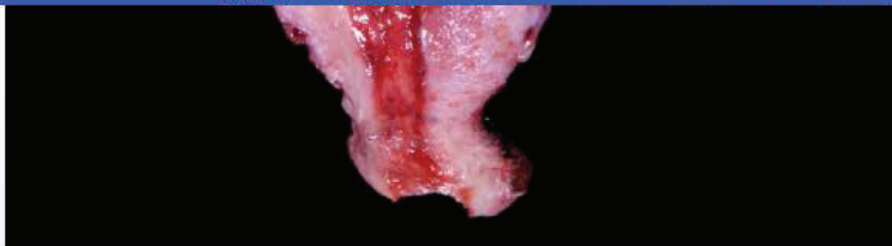
Reverse Color



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Which of the following is the most likely diagnosis?

- ☐ A. Adenomyosis
- ☐ B. Chronic endometritis
- ☐ C. Complete hydatidiform mole
- ☐ D. Endometriosis
- ☐ E. Uterine leiomyoma
- ☐ F. Uterine sarcoma

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Which of the following is the most likely diagnosis?

- ☒ A. Adenomyosis (51%)
- ☐ B. Chronic endometritis (5%)
- ☐ C. Complete hydatidiform mole (0%)
- ☐ D. Endometriosis (11%)
- ☐ E. Uterine leiomyoma (21%)
- ☐ F. Uterine sarcoma (10%)

Correct

51%  
Answered correctly

01 min, 02 secs  
Time Spent

02/13/2021  
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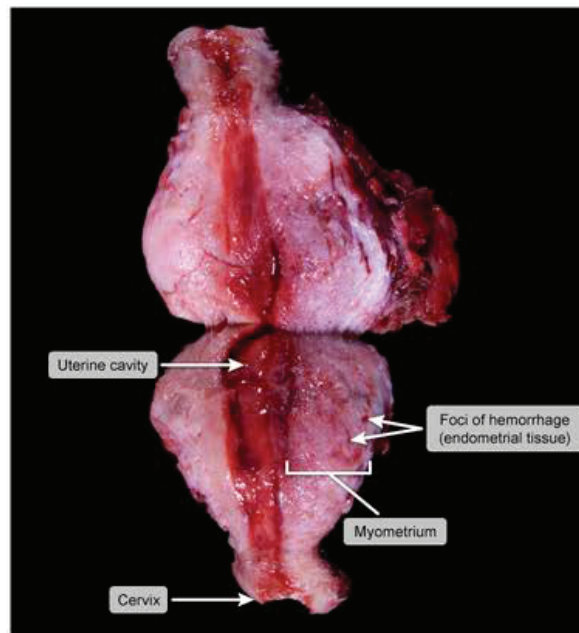
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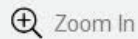
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## Exhibit Display

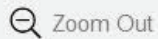
## Adenomyosis



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This patient with heavy menses and dysmenorrhea has **adenomyosis**, the abnormal presence of

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End Block





This patient with heavy menses and dysmenorrhea has **adenomyosis**, the abnormal presence of **endometrial glands and stroma** within the uterine myometrium (ie, uterine wall). Adenomyosis typically occurs in women age >40, and risk factors include multiparity and prior uterine surgery (eg, cesarean delivery).

The pathology of adenomyosis correlates with its clinical symptoms. Adenomyosis has a gross appearance as areas of **dark red endometrial tissue within the myometrium**. With each menstrual cycle, the endometrial tissue proliferates and sheds but the bleeding is confined within the uterine wall, causing **dysmenorrhea**. In addition, the ectopic endometrial glands induce **myometrial hyperplasia and hypertrophy**, creating a **globular, uniformly enlarged uterus**. This uterine enlargement also increases the surface area of the endometrial cavity, resulting in **regular, heavy menses** (eg, every 28-30 days). Definitive treatment is with hysterectomy.

**(Choice B)** Chronic endometritis is an intrauterine polymicrobial infection that typically causes constant pelvic pain with irregular bleeding rather than dysmenorrhea and regular, heavy menses. Because the disease process is intracavitary, there is no associated uterine enlargement. Gross pathology may reveal intrauterine adhesions due to chronic intrauterine inflammation.

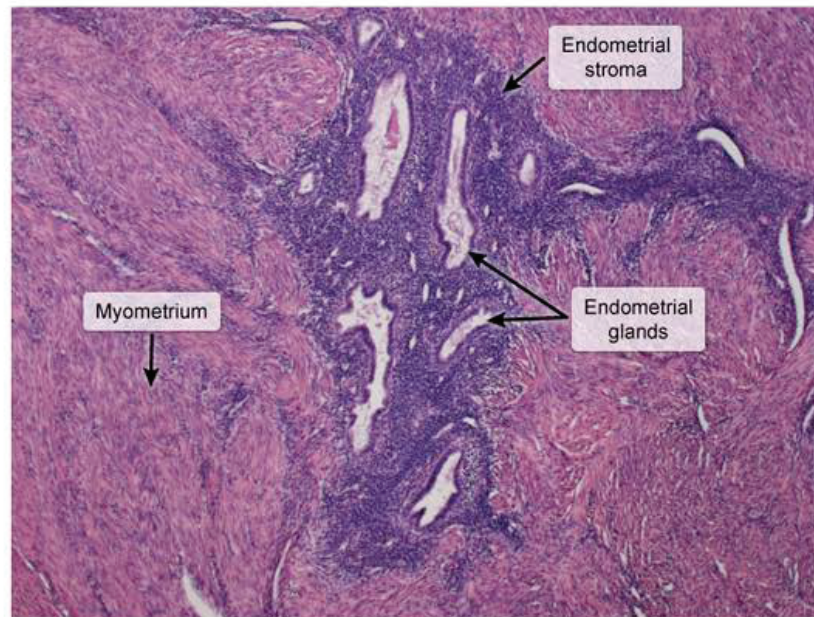
**(Choice C)** A **complete hydatidiform mole** typically causes amenorrhea or irregular, first-trimester bleeding





## Exhibit Display

## Adenomyosis



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intrauterine adhesions due to chronic intrauterine inflammation.

**(Choice C)** A **complete hydatidiform mole** typically causes amenorrhea or irregular, first-trimester bleeding rather than regular, heavy menses. In addition, patients typically have markedly elevated  $\beta$ -hCG levels (ie,  $>100,000$  mIU/mL). Gross pathology may reveal uterine enlargement, but there are typically numerous edematous intrauterine chorionic villi.

**(Choice D)** Endometriosis is a common cause of dysmenorrhea due to ectopic implantation of endometrial glands and stroma in the abdominopelvic cavity; because the ectopic implants are extrauterine, patients do not have uterine enlargement or heavy menses. Gross pathology typically reveals black powder–burn lesions or ovarian cysts (ie, **endometrioma**).

**(Choice E)** **Uterine leiomyomas** are benign, uterine smooth muscle cell tumors that can cause regular, heavy menses. However, gross pathology typically reveals an irregularly enlarged uterus with discrete tumors rather than a uniformly globular uterus.

**(Choice F)** Uterine sarcomas are malignant uterine tumors. Affected patients typically have irregular, postmenopausal bleeding rather than regular, heavy menses. Gross pathology typically reveals a discrete uterine mass.







## Exhibit Display

Complete hydatidiform mole

Edematous, grape-like  
chorionic villi

Zoom In



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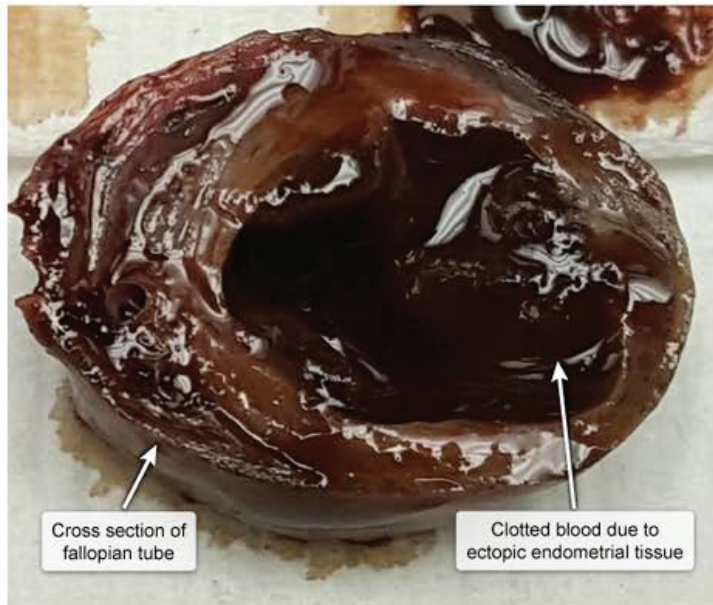
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## Exhibit Display

## Endometriosis



Cross section of  
fallopian tube

Clotted blood due to  
ectopic endometrial tissue

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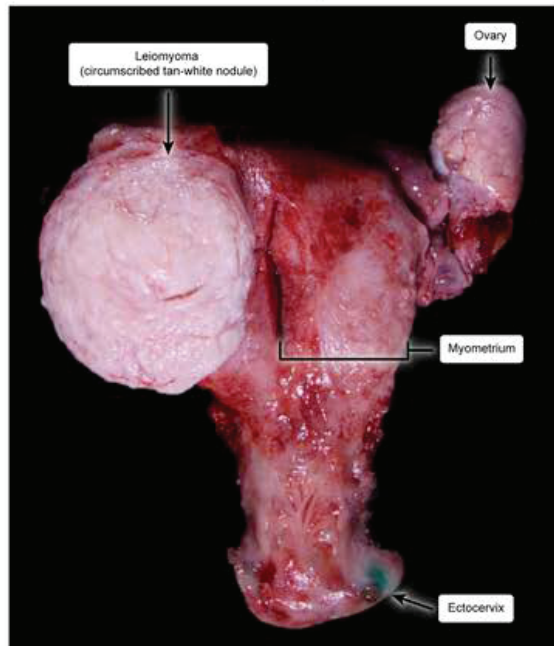
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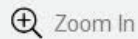
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### Exhibit Display

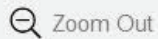
Uterine leiomyoma



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**(Choice D)** Endometriosis is a common cause of dysmenorrhea due to ectopic implantation of endometrial glands and stroma in the abdominopelvic cavity; because the ectopic implants are extrauterine, patients do not have uterine enlargement or heavy menses. Gross pathology typically reveals black powder–burn lesions or ovarian cysts (ie, [endometrioma](#)).

**(Choice E)** [Uterine leiomyomas](#) are benign, uterine smooth muscle cell tumors that can cause regular, heavy menses. However, gross pathology typically reveals an irregularly enlarged uterus with discrete tumors rather than a uniformly globular uterus.

**(Choice F)** Uterine sarcomas are malignant uterine tumors. Affected patients typically have irregular, postmenopausal bleeding rather than regular, heavy menses. Gross pathology typically reveals a discrete uterine mass.

### Educational objective:

Adenomyosis typically presents with regular (ie, cyclic), heavy, painful menses. Gross pathology reveals a uniformly enlarged, globular uterus with the abnormal presence of endometrial glands and stroma in the myometrium.

### References

- [Adenomyosis: what is new?](#)





A 39-year-old, nulliparous woman comes to the office due to pelvic pressure and constipation that have worsened over the past year. She frequently has an uncomfortable sensation of incomplete evacuation following defecation. Menses occur every 28 days without heavy bleeding or severe pain. The patient has no pain with intercourse and routinely uses condoms for contraception. BMI is 24 kg/m<sup>2</sup>. Examination shows an irregularly enlarged uterus and normal rectal tone. Which of the following is the most likely etiology of the patient's constipation?

- ☐ A. Adenomyosis
- ☐ B. Cervical carcinoma
- ☐ C. Posterior subserosal uterine leiomyoma
- ☐ D. Posterior vaginal wall prolapse
- ☐ E. Rectovaginal endometriosis

Submit





A 39-year-old, nulliparous woman comes to the office due to pelvic pressure and constipation that have worsened over the past year. She frequently has an uncomfortable sensation of incomplete evacuation following defecation. Menses occur every 28 days without heavy bleeding or severe pain. The patient has no pain with intercourse and routinely uses condoms for contraception. BMI is 24 kg/m<sup>2</sup>. Examination shows an irregularly enlarged uterus and normal rectal tone. Which of the following is the most likely etiology of the patient's constipation?

- ☐ A. Adenomyosis (8%)
- ☐ B. Cervical carcinoma (0%)
- ☒ C. Posterior subserosal uterine leiomyoma (73%)
- ☐ D. Posterior vaginal wall prolapse (8%)
- ☐ E. Rectovaginal endometriosis (8%)

Correct



73%

Answered correctly



48 secs

Time Spent



11/04/2020

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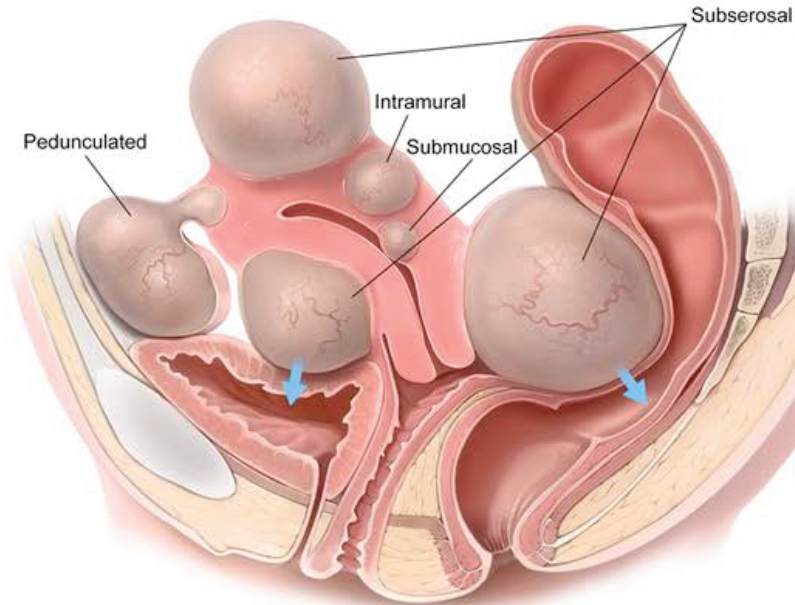


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### Exhibit Display

#### Uterine fibroids



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This patient with constipation, pelvic pressure, and an irregularly enlarged uterus likely has a **uterine leiomyoma**. Leiomyomas (ie, fibroids) are monoclonal tumors; each fibroid is derived from a distinct progenitor cell. They can be located on the serosal surface of the uterus (subserosal), within the uterine wall (intramural), and beneath the endometrium (submucosal).

Subserosal fibroids typically cause greater uterine irregularity and enlargement compared to intramural or submucosal fibroids, which are more constrained by uterine tissue. Because the uterus is located posterior to the bladder and anterior to the rectosigmoid colon, **irregular uterine enlargement** from fibroids can put pressure on these adjacent organs, causing bulk-related symptoms (eg, **pelvic pressure**). Fibroids in the **posterior uterus** can put pressure on the **colon**, leading to **constipation**.

Additional symptoms vary, depending on location. Anterior subserosal fibroids may cause obstructive urinary symptoms (eg, urgency, incomplete emptying). Other types (eg, submucosal or intramural) can lead to reproductive difficulties due to distortion of the endometrial cavity. Submucosal fibroids in particular can cause prolonged and/or heavy menstrual bleeding.

**(Choice A)** Adenomyosis typically presents with dysmenorrhea, heavy menstrual bleeding, and a diffusely tender, **uniformly globular uterus** rather than an irregularly enlarged uterus. It is not associated with



can cause prolonged and/or heavy menstrual bleeding.

**(Choice A)** Adenomyosis typically presents with dysmenorrhea, heavy menstrual bleeding, and a diffusely tender, **uniformly globular uterus** rather than an irregularly enlarged uterus. It is not associated with constipation.

**(Choice B)** Advanced-stage cervical cancer may cause bulk-related symptoms such as constipation and pelvic pressure. However, patients typically have abnormal bleeding (eg, postcoital bleeding) or a visible cervical lesion.

**(Choice D)** Pelvic organ prolapse is the herniation of pelvic structures through the vagina due to pelvic floor weakening. Although **posterior vaginal wall prolapse** (ie, rectocele) can cause pelvic pressure and constipation, it does not cause uterine enlargement. In addition, premenopausal, nonobese, nulliparous women are at low risk for pelvic organ prolapse.

**(Choice E)** Rectovaginal **endometriosis**, ectopic implants of endometrial glands and stroma, may cause pelvic pain and constipation, especially around menses. However, dyspareunia (ie, pain with intercourse), dyschezia, and a palpable, tender nodularity are typically present.

**Educational objective:**

Subserosal uterine leiomyomas (fibroids) can cause irregular uterine enlargement and bulk-related





cervical lesion.

**(Choice D)** Pelvic organ prolapse is the herniation of pelvic structures through the vagina due to pelvic floor weakening. Although [posterior vaginal wall prolapse](#) (ie, rectocele) can cause pelvic pressure and constipation, it does not cause uterine enlargement. In addition, premenopausal, nonobese, nulliparous women are at low risk for pelvic organ prolapse.

**(Choice E)** Rectovaginal [endometriosis](#), ectopic implants of endometrial glands and stroma, may cause pelvic pain and constipation, especially around menses. However, dyspareunia (ie, pain with intercourse), dyschezia, and a palpable, tender nodularity are typically present.

### Educational objective:

Subserosal uterine leiomyomas (fibroids) can cause irregular uterine enlargement and bulk-related symptoms (eg, pelvic pressure). Posterior leiomyomas can cause constipation due to pressure on the colon.

### References

- [Uterine fibroids: diagnosis and treatment.](#)





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Lab Values



Notes



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Text Zoom



Settings

A 34-year-old woman comes to the office for follow-up after 2 abnormal Papanicolaou test results. The patient has had 4 lifetime sex partners, uses oral contraceptive pills, and has never been pregnant. She has no other medical problems and does not use tobacco, alcohol, or illicit drugs. Her mother has breast cancer. Physical examination is normal. A cervical biopsy reveals high-grade cervical intraepithelial neoplasia. Which of the following is the most likely finding on histopathology?

- ☐ A. Atypical glandular elements invading the basement membrane
- ☐ B. Cells with nuclear atypia only in the basal epithelial layer
- ☐ C. Expansion of immature basal cells to the epithelial surface
- ☐ D. Nests of atypical cells in the subepithelial stroma
- ☐ E. Suprabasilar cells with perinuclear vacuolization only

**Submit**

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Lab Values



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Text Zoom






Settings

A 34-year-old woman comes to the office for follow-up after 2 abnormal Papanicolaou test results. The patient has had 4 lifetime sex partners, uses oral contraceptive pills, and has never been pregnant. She has no other medical problems and does not use tobacco, alcohol, or illicit drugs. Her mother has breast cancer. Physical examination is normal. A cervical biopsy reveals high-grade cervical intraepithelial neoplasia. Which of the following is the most likely finding on histopathology?

- ☐ A. Atypical glandular elements invading the basement membrane (13%)
- ☐ B. Cells with nuclear atypia only in the basal epithelial layer (15%)
- ☒ C. Expansion of immature basal cells to the epithelial surface (53%)
- ☐ D. Nests of atypical cells in the subepithelial stroma (11%)
- ☐ E. Suprabasilar cells with perinuclear vacuolization only (5%)

Correct

 53%  
Answered correctly 01 min, 17 secs  
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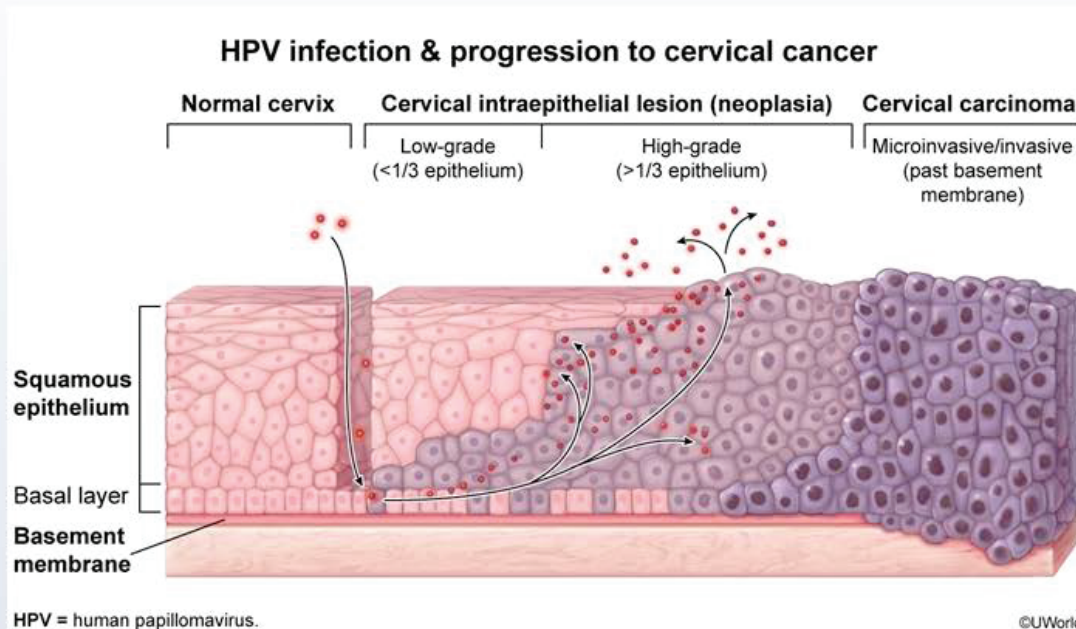


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**Human papillomavirus (HPV)** infection of basal cervical cells can progress to malignancy. Cervical cancer screening is initially done with cervical cytology in Papanicolaou (Pap) tests, which sometimes leads to further evaluation (eg, colposcopy, biopsy) if certain squamous or glandular abnormalities are seen.



**Human papillomavirus (HPV)** infection of basal cervical cells can progress to malignancy. Cervical cancer screening is initially done with cervical cytology in Papanicolaou (Pap) tests, which sometimes leads to further evaluation (eg, colposcopy, biopsy) if certain squamous or glandular abnormalities are seen.

This patient had 2 abnormal Pap test results and now has a biopsy showing **cervical intraepithelial neoplasia (CIN)**, which indicates one of the following types of **squamous** abnormalities:

- **High-grade CIN** (high-grade squamous intraepithelial lesions [HSILs]) means that the atypical cells have invaded **beyond the lower one-third** of the cervical epithelium (eg, to the **epithelial surface**), as seen on this patient's biopsy. HSILs have a high rate of progression to cancer.
- Low-grade CIN (low-grade squamous intraepithelial lesions [LSILs]) means that the cells have not invaded past the lower one-third of the cervical epithelium. In most cases, LSILs regress spontaneously (**Choice B**).

**(Choices A and D)** Basement membrane invasion (eg, atypical cells in subepithelial stroma) signifies carcinoma. When atypical glandular cells (originating from the endocervix) are seen on Pap tests, a biopsy is often required and can reveal squamous CIN, despite the original glandular findings.

**(Choice E)** HPV infection can cause perinuclear vacuolization (koilocytic change) due to viral proteins. This does not reflect any malignant or premalignant conditions.





spontaneously (**Choice B**).

**(Choices A and D)** Basement membrane invasion (eg, atypical cells in subepithelial stroma) signifies carcinoma. When atypical glandular cells (originating from the endocervix) are seen on Pap tests, a biopsy is often required and can reveal squamous CIN, despite the original glandular findings.

**(Choice E)** HPV infection can cause perinuclear vacuolization (koilocytic change) due to viral proteins. This does not reflect any malignant or premalignant conditions.

### Educational objective:

Human papillomavirus infection of basal cervical cells can progress to premalignant and cancerous lesions. Cervical intraepithelial neoplasia refers to atypical squamous cells and is classified as low-grade squamous intraepithelial lesions (if extending  $<1/3$  of the epithelium) or high-grade squamous intraepithelial lesions (if extending beyond). Basement membrane breach signifies invasive disease.

### References

- The Pap Test and Bethesda 2014. "The reports of my demise have been greatly exaggerated." (after a quotation from Mark Twain).
- A fusion-based approach for uterine cervical cancer histology image classification.







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Settings

A 34-year-old woman with polycystic ovary syndrome comes to the office with her husband for treatment of infertility. The patient has been unable to conceive despite having unprotected sexual intercourse several times a week for the past 2 years. Her menses are irregular and occur every 2-3 months, consistent with chronic anovulation. She does not use tobacco, alcohol, or illicit drugs. The patient takes no medications and has no allergies. BMI is 32 kg/m<sup>2</sup>. Physical examination shows coarse hair on her chin and abdomen. The patient is initially prescribed clomiphene therapy but fails to conceive. She then receives ovulation induction therapy with a short course of menotropins followed by a single injection of human chorionic gonadotropin (hCG). The use of hCG therapy primarily mimics which of the following physiologic events?

- ☐ A. Estrogen surge
- ☐ B. FSH surge
- ☐ C. LH surge
- ☒ D. Progesterone surge
- ☐ E. Prolactin surge



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Settings

infertility. The patient has been unable to conceive despite having unprotected sexual intercourse several times a week for the past 2 years. Her menses are irregular and occur every 2-3 months, consistent with chronic anovulation. She does not use tobacco, alcohol, or illicit drugs. The patient takes no medications and has no allergies. BMI is 32 kg/m<sup>2</sup>. Physical examination shows coarse hair on her chin and abdomen. The patient is initially prescribed clomiphene therapy but fails to conceive. She then receives ovulation induction therapy with a short course of menotropins followed by a single injection of human chorionic gonadotropin (hCG). The use of hCG therapy primarily mimics which of the following physiologic events?

- ☐ A. Estrogen surge (3%)
- ☐ B. FSH surge (4%)
- ☒ C. LH surge (64%)
- ☐ D. Progesterone surge (26%)
- ☐ E. Prolactin surge (0%)

Correct

64%



31 secs



12/10/2020

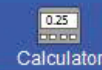
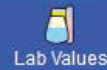
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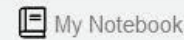
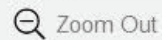
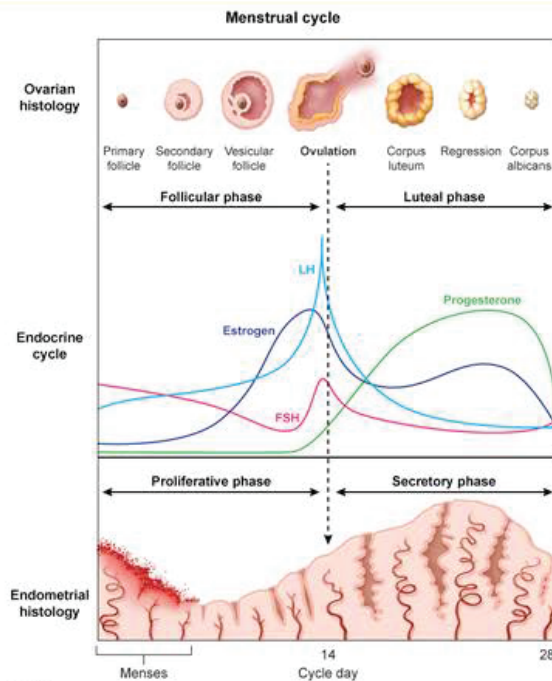
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Women of reproductive age experience cyclic hormonal changes of the hypothalamus-pituitary-ovarian axis that normally manifest as monthly ovulation and menstrual bleeding. Pulsatile gonadotropin-releasing hormone from the hypothalamus causes intermittent secretion of FSH and LH from the pituitary. FSH and LH are responsible for the development of the ovarian follicle and ovulation, respectively.

The normal menstrual cycle consists of the follicular and luteal phases. Following the onset of menstruation, FSH stimulates one or more dominant follicles to form in one of the ovaries (follicular phase). FSH also stimulates estrogen production from the ovaries. As the follicular phase advances, a progressive rise in serum estradiol is seen. High estrogen levels in the late follicular phase have a positive feedback effect on LH production, resulting in an LH surge. Ultimately, the **LH surge** causes the rupture of the dominant follicle, leading to extrusion of an ovum (ovulation).

Failure of ovulation (eg, anovulation in polycystic ovary syndrome) is a common cause of infertility. Treatment options include the administration of drugs that act like FSH and LH. Menotropin (human menopausal gonadotrophin) therapy mimics FSH and triggers the formation of a dominant ovarian follicle. When the follicle appears mature, exogenous **human chorionic gonadotropin (hCG)** is administered. The alpha subunit of hCG is structurally similar to LH and therefore simulates the LH surge by **inducing**





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ovulation.

**(Choice A)** Estrogen levels continue to increase progressively during the follicular phase. Peak estrogen levels are seen just before the LH surge.

**(Choice B)** The effect of hCG therapy is analogous to the LH surge. Menotropin therapy mimics the FSH surge, which is very small compared to the large LH surge.

**(Choice D)** Progesterone secretion increases following ovulation with the formation of the corpus luteum. Peak progesterone levels are seen in the mid-luteal phase.

**(Choice E)** Prolactin increases substantially during pregnancy and peaks at delivery to prepare the breast for lactation. Elevated prolactin levels lead to anovulation (eg, lactational amenorrhea).

### Educational objective:

Anovulation is a common cause of infertility. Menotropin (human menopausal gonadotropin) is a treatment option that acts like FSH and triggers the formation of a dominant ovarian follicle. Ovulation is then induced by administration of human chorionic gonadotropin, which mimics the LH surge.

### References

- [Ovulation triggers in anovulatory women undergoing ovulation induction.](#)



0



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Lab Values



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Settings

A 28-year-old woman comes to the office due to discomfort during urination for the past 3 months.

Antibiotics for a urinary tract infection were prescribed at an urgent care center a few weeks ago, but her symptoms have persisted despite treatment. The patient has also noticed increasing pain with the passage of stool for the last year, particularly during menses. Bowel movements occur daily and are soft and not watery. Examination shows suprapubic tenderness and an immobile, retroverted uterus. Rectovaginal examination reveals nodularity in the posterior cul-de-sac. Urinalysis and urine culture are normal.

Surgical biopsy of the pelvic nodules would most likely show which of the following?

- ☐ A. Colorectal hamartoma
- ☐ B. Endometrial glands and stroma
- ☐ C. Endometrial intraepithelial neoplasia
- ☐ D. Invasive urothelial carcinoma
- ☒ E. Serous epithelial ovarian carcinoma
- ☐ F. Uterine myometrium



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Feedback



Suspend



End Block





Antibiotics for a urinary tract infection were prescribed at an urgent care center a few weeks ago, but her symptoms have persisted despite treatment. The patient has also noticed increasing pain with the passage of stool for the last year, particularly during menses. Bowel movements occur daily and are soft and not watery. Examination shows suprapubic tenderness and an immobile, retroverted uterus. Rectovaginal examination reveals nodularity in the posterior cul-de-sac. Urinalysis and urine culture are normal. Surgical biopsy of the pelvic nodules would most likely show which of the following?

- ☐ A. Colorectal hamartoma (1%)
- ☒ B. Endometrial glands and stroma (75%)
- ☐ C. Endometrial intraepithelial neoplasia (4%)
- ☐ D. Invasive urothelial carcinoma (2%)
- ☐ E. Serous epithelial ovarian carcinoma (1%)
- ☐ F. Uterine myometrium (13%)

Correct

75%  
Answered correctly01 min, 23 secs  
Time Spent09/05/2020  
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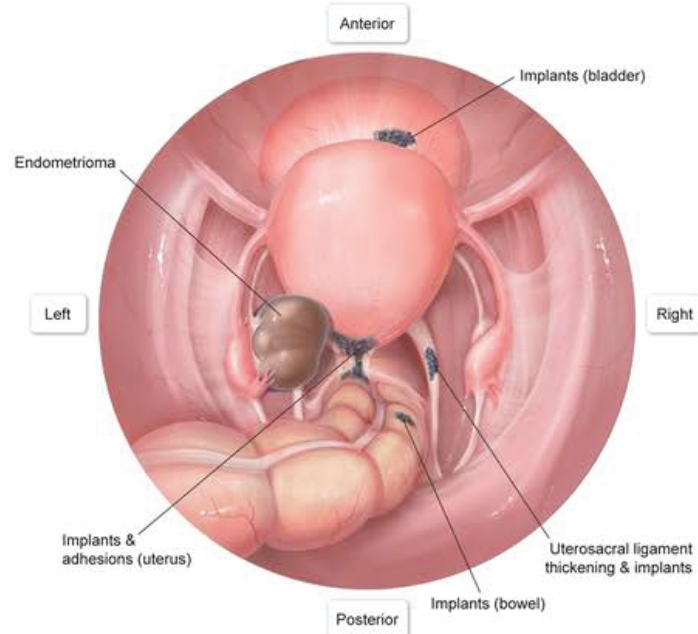
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## Exhibit Display

## Pelvic endometriosis



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1



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**Endometriosis** affects women of reproductive age and is characterized by the **ectopic implantation of endometrial glands and stroma**, causing chronic pelvic pain. Symptoms and examination findings vary, depending on the specific location of endometriosis implants.

**Dysuria** or suprapubic tenderness and **dyschezia** (pain with defecation) can be caused by implants on the bladder and rectovaginal septum, respectively. Bowel symptoms commonly worsen with menses.

**Rectovaginal nodularity** is highly characteristic of endometrial implants and fibrosis of the posterior cul-de-sac. The uterus is often immobile and fixed in a retroverted position due to scarring from continued cyclic shedding of ectopic endometrial tissue that has no outlet. Other common clinical features include an adnexal mass (endometrioma) and cervical motion tenderness. Definitive diagnosis is by direct visualization with biopsy during surgical exploration.

**(Choice A)** Colorectal hamartomas, typically benign colonic tumors, may cause abdominal pain due to mass effect; however, hamartomas do not worsen with menses or cause pelvic inflammation (eg, immobile uterus).

**(Choice C)** Endometrial intraepithelial neoplasia, atypical overgrowth of the intrauterine endometrial lining, typically occurs in women with risk factors (eg, obesity, chronic anovulation). Patients typically have



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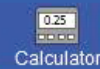
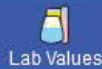


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uterus).

**(Choice C)** Endometrial intraepithelial neoplasia, atypical overgrowth of the intrauterine endometrial lining, typically occurs in women with risk factors (eg, obesity, chronic anovulation). Patients typically have abnormal uterine bleeding or postmenopausal bleeding.

**(Choice D)** Invasive urothelial carcinoma can cause dysuria, but patients typically have painless hematuria; this patient's urinalysis is normal, making this diagnosis unlikely.

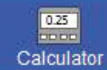
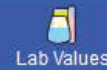
**(Choice E)** Serous epithelial ovarian carcinoma can cause abdominal pain, but the typical presentation is bloating or ascites in a postmenopausal patient with an adnexal mass.

**(Choice F)** **Leiomyoma** (ie, fibroids), benign tumors of uterine myometrium, may cause abdominal pain and urinary or bowel symptoms due to mass effect; however, symptomatic patients typically have an irregularly enlarged uterus, making this diagnosis less likely.

**Educational objective:**

Endometriosis causes chronic pelvic pain due to ectopic implantation of endometrial glands and stroma in the abdominopelvic cavity. Bladder implants may also result in dysuria while rectovaginal implants may cause dyschezia, rectovaginal nodularity, and pelvic fibrosis (eg, immobile uterus).





A 17-year-old girl comes to the office with her mother for evaluation of urinary frequency and urgency. She has also noticed scant vaginal discharge. The symptoms started 2 days ago. The patient has never had similar symptoms before and has no chronic medical problems. She takes a combination oral contraceptive daily and has been sexually active with multiple partners over the last year. She is a high school student and does not use tobacco or alcohol. A urine sample is obtained for urinalysis and culture. Which of the following additional findings would be most specific for a diagnosis of pyelonephritis?

- ☐ A. Abdominal pain
- ☐ B. Bacteriuria
- ☐ C. Fever
- ☐ D. Microscopic hematuria
- ☐ E. Sterile pyuria
- ☐ F. White blood cell casts

**Submit**

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Reverse Color



Text Zoom



Settings

A 17-year-old girl comes to the office with her mother for evaluation of urinary frequency and urgency. She has also noticed scant vaginal discharge. The symptoms started 2 days ago. The patient has never had similar symptoms before and has no chronic medical problems. She takes a combination oral contraceptive daily and has been sexually active with multiple partners over the last year. She is a high school student and does not use tobacco or alcohol. A urine sample is obtained for urinalysis and culture. Which of the following additional findings would be most specific for a diagnosis of pyelonephritis?

- ☒ A. Abdominal pain (0%)
- ☐ B. Bacteriuria (5%)
- ☐ C. Fever (10%)
- ☐ D. Microscopic hematuria (2%)
- ☐ E. ~~Sterile pyuria~~ (3%)
- ☒ F. White blood cell casts (77%)



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Settings

Women are more susceptible to urinary tract infections (UTIs) as their urethra is both closer to the rectum and shorter than that of men. Sexual intercourse is often a precipitating factor for UTIs.

Urethritis and cystitis are both characterized by dysuria, frequency, urgency, pyuria, and bacteriuria, but suprapubic pressure and tenderness is more specific to cystitis. If pathogens ascend via the ureter to penetrate the kidney parenchyma, symptoms of acute **pyelonephritis** including fever, chills, nausea, vomiting, flank/abdominal pain, and costovertebral angle tenderness develop. Urine sediment microscopy reveals white blood cells (WBCs), **WBC casts**, and bacteria.

Pyuria and bacteriuria are also found in infections of the lower urinary tract, but WBC casts are pathognomonic for pyelonephritis in the setting of UTI. They are formed only in tubules, where WBCs precipitate with Tamm-Horsfall protein secreted by tubular epithelial cells. WBC casts can also be seen with acute interstitial nephritis, which often presents with low-grade fever and findings of acute kidney injury (urinary symptoms are not present).

**(Choices A and C)** Fever (a sign of any systemic infection) and abdominal pain are nonspecific symptoms. They can be present in acute pyelonephritis and in numerous other conditions, such as pelvic inflammatory disease. Mild/moderate urinary symptoms can also occur with pelvic infection/inflammation of



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**(Choices A and C)** Fever (a sign of any systemic infection) and abdominal pain are nonspecific

symptoms. They can be present in acute pyelonephritis and in numerous other conditions, such as pelvic inflammatory disease. Mild/moderate urinary symptoms can also occur with pelvic infection/inflammation of any cause.

**(Choices B and D)** Bacteriuria and microscopic hematuria are found in both upper (acute pyelonephritis) and lower (cystitis, urethritis) UTIs.

**(Choice E)** Sterile pyuria (WBCs, but no bacteria) occurs in a small number of patients with acute pyelonephritis, but it can also be seen with nongonococcal urethritis caused by *Chlamydia* or *Ureaplasma*.

### Educational objective:

Pyuria and bacteriuria are found in both upper and lower urinary tract infections (UTIs). However, white blood cell casts only form in the renal tubules and are pathognomonic for acute pyelonephritis when accompanied by symptoms of acute UTI.

Pathology

Female Reproductive System &amp; Breast

Urinary tract infection

Subject

System

Topic

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Settings

A 73-year-old woman, gravida 0 para 0, comes to the office due to breathing difficulty and increasing abdominal girth. She also has decreased appetite and constipation that has worsened progressively for the last 6 months. The patient has no other medical conditions and has not seen a health care provider in several years. On physical examination, the abdomen is distended and nontender with right adnexal fullness. She undergoes laparoscopic surgical evaluation for a right adnexal mass. Microscopic examination of the surgical biopsy specimen reveals anaplasia of epithelial cells with invasion into the stroma and multiple papillary formations with cellular atypia, as shown in the [exhibit](#). Which of the following is most likely to be elevated in this patient?

- ☐ A.  $\alpha$ -fetoprotein
- ☐ B.  $\beta$ -hCG
- ☐ C. CA-125
- ☐ D. Estrogen
- ☐ E. Inhibin
- ☐ F. LDH



1



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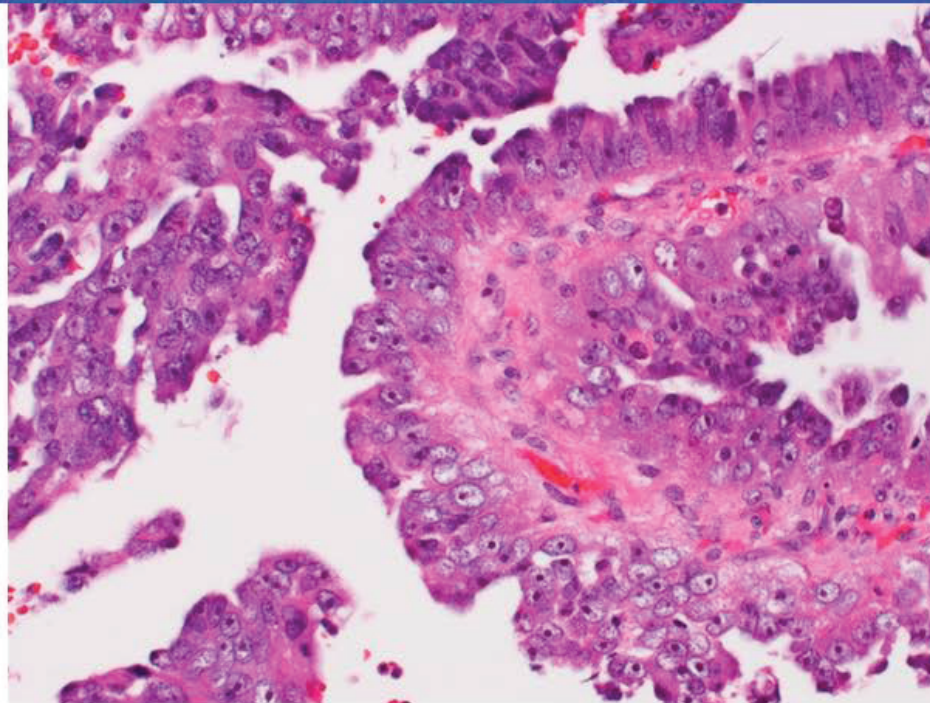
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Exhibit Display



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abdominal girth. She also has decreased appetite and constipation that has worsened progressively for the last 6 months. The patient has no other medical conditions and has not seen a health care provider in several years. On physical examination, the abdomen is distended and nontender with right adnexal fullness. She undergoes laparoscopic surgical evaluation for a right adnexal mass. Microscopic examination of the surgical biopsy specimen reveals anaplasia of epithelial cells with invasion into the stroma and multiple papillary formations with cellular atypia, as shown in the [exhibit](#). Which of the following is most likely to be elevated in this patient?

- ☐ A.  $\alpha$ -fetoprotein
- ☐ B.  $\beta$ -hCG
- ☐ C. CA-125
- ☐ D. Estrogen
- ☐ E. Inhibin
- ☐ F. LDH
- ☐ G. Testosterone





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Settings

several years. On physical examination, the abdomen is distended and nontender with right adnexal

fullness. She undergoes laparoscopic surgical evaluation for a right adnexal mass. Microscopic examination of the surgical biopsy specimen reveals anaplasia of epithelial cells with invasion into the stroma and multiple papillary formations with cellular atypia, as shown in the [exhibit](#). Which of the following is most likely to be elevated in this patient?

- ☐ A.  $\alpha$ -fetoprotein (5%)
- ☐ B.  $\beta$ -hCG (6%)
- ☒ C. CA-125 (76%)
- ☐ D. Estrogen (6%)
- ☐ E. Inhibin (1%)
- ☐ F. LDH (2%)
- ☐ G. Testosterone (0%)

Correct

76%  
Answered correctly01 min, 25 secs  
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## Malignant ovarian neoplasms

Histologic type	Diagnosis	Key features
Epithelial	Serous cystadenocarcinoma	<ul style="list-style-type: none"><li>• Most common ovarian cancer</li><li>• Often bilateral</li><li>• Histology: Psammoma bodies</li></ul>
	Mucinous cystadenocarcinoma	<ul style="list-style-type: none"><li>• Pseudomyxoma peritonei</li><li>• Mucin-producing epithelial cells</li></ul>
Germ cell	Dysgerminoma	<ul style="list-style-type: none"><li>• Adolescents</li><li>• ↑ <math>\beta</math>-hCG, ↑ LDH</li><li>• Histology: "Fried egg cells"</li></ul>
	Endodermal sinus (yolk sac)	<ul style="list-style-type: none"><li>• ↑ AFP</li><li>• Aggressive</li><li>• Schiller-Duval bodies resemble glomeruli</li></ul>

Stroma (sex cord)	Granulosa cell	<ul style="list-style-type: none"><li>• ↑ Estrogen (eg, endometrial hyperplasia, postmenopausal bleeding)</li><li>• ↑ Inhibin</li><li>• Histology: Call-Exner bodies, coffee bean nuclei</li></ul>
	Sertoli-Leydig	<ul style="list-style-type: none"><li>• ↑ Androgens (eg, hirsutism, clitoromegaly)</li></ul>

**AFP** = alpha-fetoprotein; **LDH** = lactate dehydrogenase.

This patient has **ovarian cancer**, which has 3 histologic types: epithelial, germ cell, and sex cord stroma.

**Epithelial** ovarian cancer is the most common subtype and is associated with increased levels of cancer antigen 125 (**CA-125**).

CA-125 is a protein expressed by epithelial cells lining the reproductive tract (eg, ovary, fallopian tubes) and the peritoneum. Epithelial ovarian cancers can secrete CA-125, allowing it to be used as a **tumor marker**. However, numerous benign conditions that disrupt the epithelial cell membrane (eg, endometriosis) can also cause increased release of CA-125 into the bloodstream, making it unsuitable for cancer screening but useful for diagnosis and treatment follow-up.

Patients with ovarian cancer typically present with a pelvic mass, ascites, and peritoneal metastasis that



Patients with ovarian cancer typically present with a pelvic mass, ascites, and peritoneal metastasis that result in decreased appetite, abdominal distension, and bowel or bladder changes (eg, constipation, urinary frequency). Nulliparous women are at increased risk for ovarian cancer due to frequent ovulation, resulting in continued disruption and repair of the ovarian epithelium. Histologic findings of **epithelial ovarian cancer** include anaplasia of epithelial cells with invasion into the stroma, multiple papillary formations with cellular atypia (arrow), and occasional Psammoma bodies.

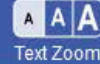
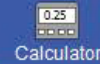
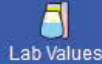
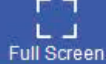
**(Choice A)** Serum  $\alpha$ -fetoprotein levels may be increased in patients with hepatocellular carcinoma and ovarian germ cell tumors (eg, endodermal sinus [yolk sac] tumor). Endodermal sinus tumors of the ovary demonstrate **Schiller-Duval bodies**, which resemble glomeruli (arrow).

**(Choices B and F)**  $\beta$ -hCG is elevated in normal pregnancy, gestational trophoblastic disease (eg, molar pregnancy, gestational choriocarcinoma), and germ cell tumors (eg, non-gestational choriocarcinoma, dysgerminomas). Dysgerminomas may also secrete LDH and have distinctive "fried egg cells" with a large round nucleus surrounded by clear cytoplasm.

**(Choices D and E)** Granulosa cell tumors of the ovary are sex cord stromal neoplasms that secrete estrogen, along with inhibin. Pathology findings include Call-Exner bodies with atypical granulosa cells containing **coffee bean nuclei (arrows)**.







pregnancy, gestational choriocarcinoma), and germ cell tumors (eg, non-gestational choriocarcinoma, dysgerminomas). Dysgerminomas may also secrete LDH and have distinctive "fried egg cells" with a large round nucleus surrounded by clear cytoplasm.

**(Choices D and E)** Granulosa cell tumors of the ovary are sex cord stromal neoplasms that secrete estrogen, along with inhibin. Pathology findings include Call-Exner bodies with atypical granulosa cells containing **coffee bean nuclei (arrows)**.

**(Choice G)** Testosterone is secreted by **Sertoli-Leydig cell tumors** of the ovary. These rare sex cord stromal neoplasms typically appear as tubules composed of Sertoli cells (green arrow) with interspersed eosinophilic Leydig cells and surrounding fibrous stroma (black arrow).

### Educational objective:

Epithelial ovarian cancer is the most common ovarian malignancy. Histologic findings include anaplasia of epithelial cells with invasion into the stroma, along with multiple papillary formations with cellular atypia. Epithelial ovarian tumors produce CA-125, which can be used as a serum marker for this condition.

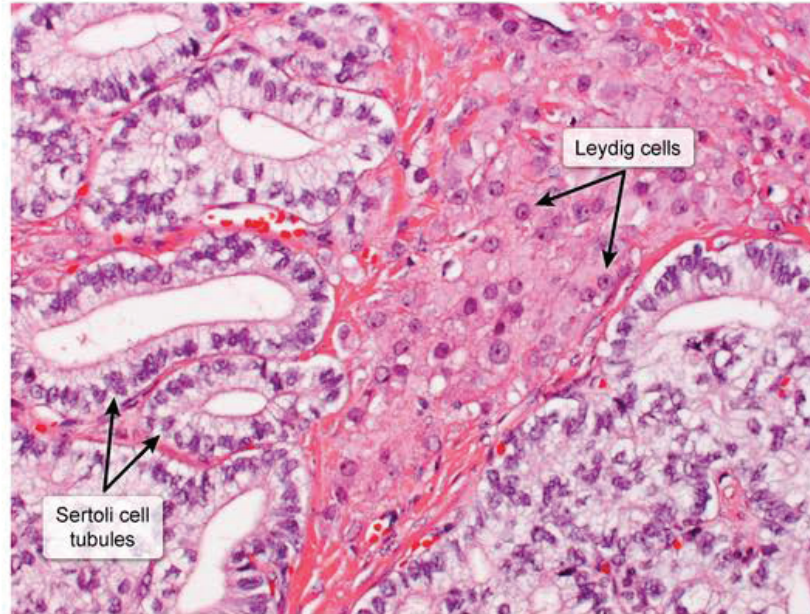
### References

- **Committee opinion no. 477: the role of the obstetrician-gynecologist in the early detection of epithelial ovarian cancer.**



Exhibit Display

Ovarian Sertoli-Leydig tumor



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A 63-year-old woman has a right-sided ovarian mass found incidentally on transvaginal ultrasound. The ultrasound revealed a normal uterus, a unilateral 3.5-cm complex ovarian mass with cystic and solid components, and no free fluid in the pelvis. The patient has no abdominal pain, changes in bowel or bladder habits, increased abdominal girth or bloating, or early satiety. Family history for ovarian cancer is negative. Physical examination shows a soft, nontender abdomen, small uterus, nonpalpable left adnexa, and enlarged, mobile right adnexa. Surgery is planned to remove the right ovary, including the mass. To avoid excessive bleeding during the oophorectomy, the surgeon should ligate which of the following structures?

- ☐ A. Mesosalpinx
- ☐ B. Ovarian ligament
- ☐ C. Round ligament of the uterus
- ☐ D. Suspensory ligament of the ovary
- ☐ E. Transverse cervical ligament







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ultrasound revealed a normal uterus, a unilateral 3.5-cm complex ovarian mass with cystic and solid components, and no free fluid in the pelvis. The patient has no abdominal pain, changes in bowel or bladder habits, increased abdominal girth or bloating, or early satiety. Family history for ovarian cancer is negative. Physical examination shows a soft, nontender abdomen, small uterus, nonpalpable left adnexa, and enlarged, mobile right adnexa. Surgery is planned to remove the right ovary, including the mass. To avoid excessive bleeding during the oophorectomy, the surgeon should ligate which of the following structures?

- ☐ A. Mesosalpinx (4%)
- ☐ B. Ovarian ligament (18%)
- ☐ C. Round ligament of the uterus (13%)
- ☒ D. Suspensory ligament of the ovary (62%)
- ☐ E. Transverse cervical ligament (1%)

Correct

62%



22 secs



09/26/2020

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Ureter

Rectum

Common iliac artery

The broad ligament is a sheet of peritoneum that extends from the lateral uterine body and upper cervix to the pelvic sidewall. It is subdivided according to the following associated reproductive structures:

- The mesosalpinx (descends from the fallopian tube)
- The mesoovarium (inferior to the mesosalpinx, covers the ovarian hilum)
- The mesometrium (inferior to the mesoovarium, extends from the lateral uterine body to the external iliac vessels and the proximal part of the round ligament)

The ovaries, located posterolaterally to the uterus, are suspended by the mesoovarium superiorly, the ovarian ligament medially, and the **suspensory ligament of the ovary** (also known as the **infundibulopelvic ligament**) laterally. The suspensory ligament of the ovary is a **fold of peritoneum** that attaches the ovary to the pelvic sidewall and **contains the ovarian artery** (major ovarian blood supply arising from the abdominal aorta entering the ovary at the hilum), **vein, lymphatics, and nerves**. The suspensory ligament of the ovary must be ligated to prevent heavy ovarian bleeding in an oophorectomy.

The ureter is in close proximity to the suspensory ligament of the ovary (medial at the level of the bifurcation of the common iliac artery). The ureter must be identified prior to ligation to avoid inadvertent ureteral transection.



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ureteral transection.

**(Choice A)** The mesosalpinx is in the region of the broad ligament below the fallopian tubes, and it does not contain the major vascular supply to the ovary. An opening is made within a nonvascular portion of the mesosalpinx below the isthmic portion of the fallopian tube during a tubal ligation to ligate a segment of the tube.

**(Choice B)** The ovarian ligament is a band of connective tissue and smooth muscle that courses in the broad ligament and connects the ovary to the side of the uterus just below the fallopian tubes. It does not contain any named vessels or major blood supply to the ovary.

**(Choice C)** The round ligaments of the uterus originate at the uterine fundus, anteroinferior to the fallopian tubes, coursing through the inguinal canal out to the labia majora. They contain the artery of Sampson, which rarely is a source of major bleeding. The round ligaments are clamped and divided to enter the peritoneum of the broad ligament during a hysterectomy.

**(Choice E)** The transverse cervical ligament, also known as the cardinal ligament, extends from the cervix and lateral fornix of the vagina to the lateral pelvic walls. The uterine artery courses in its superior portion, necessitating division and ligation of this ligament during a hysterectomy. It is not relevant for adnexal surgery, which does not involve these lower structures.



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**(Choice E)** The transverse cervical ligament, also known as the cardinal ligament, extends from the cervix and lateral fornix of the vagina to the lateral pelvic walls. The uterine artery courses in its superior portion, necessitating division and ligation of this ligament during a hysterectomy. It is not relevant for adnexal surgery, which does not involve these lower structures.

### Educational objective:

The suspensory ligament of the ovary contains the ovarian artery, vein, lymphatics, and nerves. The ovarian artery is the major blood supply to the ovary and must be ligated during an oophorectomy to prevent heavy bleeding.

### References

- [ACOG Practice Bulletin: Management of adnexal masses.](#)
- [The incidental postmenopausal adnexal mass.](#)

Anatomy

Female Reproductive System &amp; Breast

Ovarian cancer

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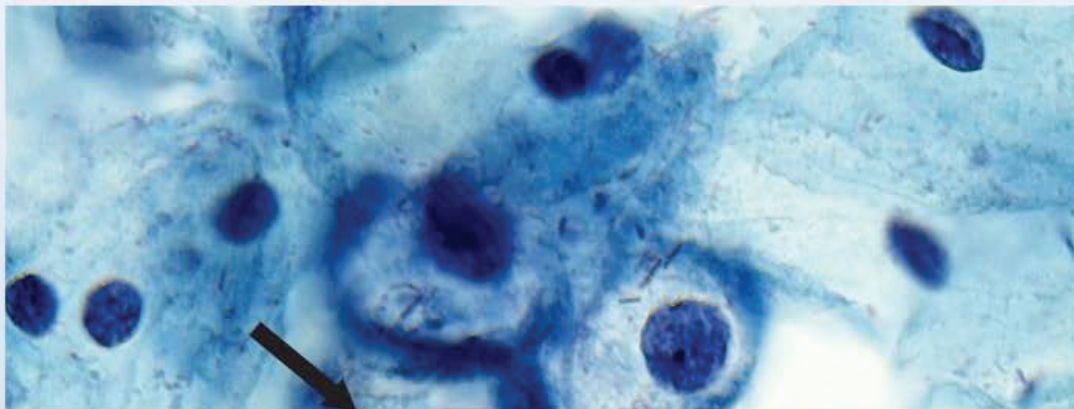
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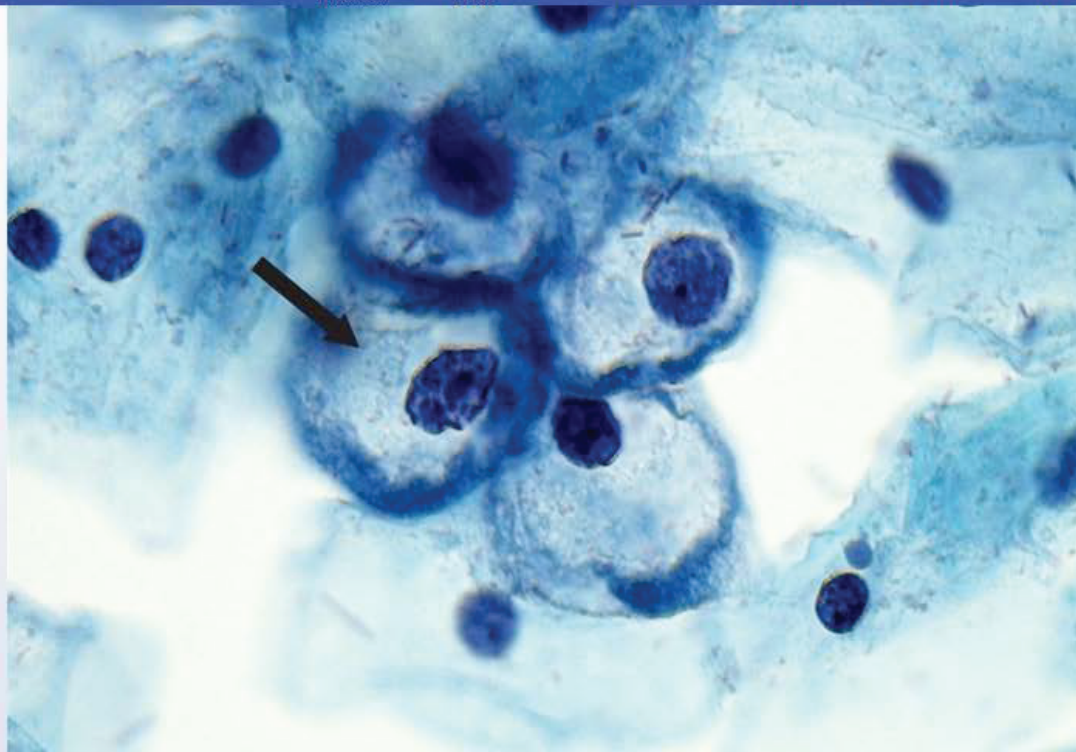
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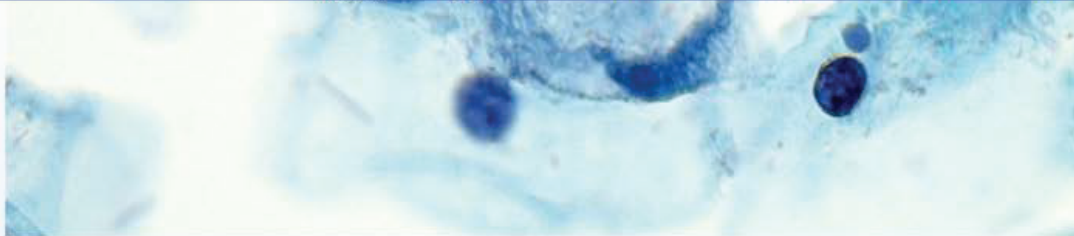
A 21-year-old woman, gravida 0, comes to the office due to postcoital bleeding. She has been sexually active with her male partner for 6 months. The patient has been taking birth control pills since age 15, when she first became sexually active. The patient and her partner do not use condoms and have never been diagnosed with a sexually transmitted infection. The patient smokes a pack of cigarettes per day. Bimanual examination reveals a small mobile uterus and no cervical motion tenderness. Speculum examination shows a well-estrogenized vagina without lesions. The cervix has an area of erythema surrounding the external os and scant clear discharge. She has her first Papanicolaou smear, and the cytological finding is shown in the image below.





Which of the following best describes the finding shown on this patient's slide?





Which of the following best describes the finding shown on this patient's slide?

- ☐ A. *Actinomyces*-like organisms
- ☐ B. *Candida albicans*
- ☐ C. Clue cell
- ☐ D. Endometrial cell
- ☐ E. Glandular cell
- ☐ F. Koilocyte
- ☐ G. Parabasal cell



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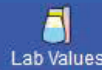
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Full Screen



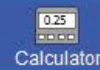
Tutorial



Lab Values



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Which of the following best describes the finding shown on this patient's slide?

- ☐ A. *Actinomyces*-like organisms (1%)
- ☐ B. *Candida albicans* (0%)
- ☒ C. Clue cell (25%)
- ☐ D. Endometrial cell (2%)
- ☐ E. Glandular cell (1%)
- ☒ F. Koilocyte (67%)
- ☐ G. Parabasal cell (1%)

**Incorrect**

Correct answer



67%

Answered correctly



21 secs

Time Spent



10/24/2020

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HPV strains	Presentation
1-4	Skin warts (verruca vulgaris)
6, 11	Genital warts (condylomata acuminata)
16, 18	Cervical, vaginal, vulvar & anal neoplasia

HPV= human papillomavirus.

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This patient's Papanicolaou (Pap) smear shows a **koilocyte**, a sign of **human papillomavirus (HPV)** infection. A koilocyte is an immature squamous cell with dense, irregularly staining cytoplasm and perinuclear clearing, resulting in a halo. It also has an enlarged pyknotic nucleus where the chromatin has condensed as part of the apoptosis process, giving it a "raisinoid" appearance.

HPV is a **double-stranded, non-enveloped DNA virus** that has a predilection for squamous epithelium of the **skin** and **vagina/cervix**. Infection with HPV may present as **warts** or **intraepithelial neoplasia**, as shown in the table above. Oncogenesis from HPV strains (eg, 16, 18) is attributed to viral proteins E6 and E7. E6 degrades p53 (tumor suppressor protein regulating the cell cycle) and E7 inhibits the retinoblastoma gene product Rb. Smoking increases the likelihood of an HPV infection developing into





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shown in the table above. Oncogenesis from HPV strains (eg, 16, 18) is attributed to viral proteins E6 and E7. E6 degrades p53 (tumor suppressor protein regulating the cell cycle) and E7 inhibits the retinoblastoma gene product Rb. Smoking increases the likelihood of an HPV infection developing into intraepithelial neoplasia and cancer.

**(Choice A)** *Actinomyces-like organisms (black arrow)* appear as clusters of basophilic thin filaments that resemble "cotton candy" on a Pap smear; their presence can be an incidental finding in patients with intrauterine devices.

**(Choice B)** *Candida albicans* is part of normal flora in many asymptomatic women. The organism can appear as pseudohyphae of budding yeast on a Pap smear.

**(Choice C)** *Clue cells* are seen in Pap smears in the setting of bacterial vaginosis, which involves a change in vaginal flora from lactobacilli to anaerobic gram-negative rods (eg, *Gardnerella vaginalis*). Clue cells are squamous cells covered with rods to obscure normal epithelial margins.

**(Choices D and E)** The endometrium consists of simple tubular glands within stroma. These cells resemble histiocytes and have small dark nuclei and no perinuclear clearing. They may be present on a Pap smear during menses. *Glandular endocervical cells (black arrow)* are columnar cells with a vacuolated or granular cytoplasm and prominent cell borders that form a honeycomb pattern when in clusters. Their



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or granular cytoplasm and prominent cell borders that form a honeycomb pattern when in clusters. Their presence in a Pap smear indicates adequate sampling.

**(Choice G)** Parabasal cells are round cells with a basophilic cytoplasm, finely granular chromatin in their nuclei, no visible nucleoli, and a high nucleus-to-chromatin ratio ("fried eggs" with a large "central egg yolk"). They predominate in Pap smears from postmenopausal and postpartum women.

### Educational objective:

Human papillomavirus (HPV) infection causes cutaneous and genital warts as well as benign and malignant intraepithelial neoplasia. Koilocytosis is a hallmark sign of HPV infection. Koilocytes are pyknotic, superficial or immature squamous cells with a dense, irregularly staining cytoplasm and perinuclear halo-like clearing.

### References

- [Clinicopathological study of Papanicolaou \(Pap\) smears for diagnosing of cervical infections.](#)

Pathology

Female Reproductive System &amp; Breast

Human papilloma virus

Subject

System

Topic

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1



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Settings

A 45-year-old woman comes to the office due to unintentional loss of 6.8 kg (15 lb) over the past 6 months. She used to enjoy dining with friends but now avoids it due to excessive lower abdominal pressure and feeling full very quickly. She also has epigastric pain but no dysphagia, regurgitation, vomiting, or diarrhea. Physical examination shows bilateral adnexal fullness. A pelvic ultrasound shows bilateral complex ovarian masses with solid and cystic components. Chest x-ray is normal. CT scan shows stomach wall thickening in addition to the ovarian masses. Which of the following is most likely to be seen on histologic evaluation of the ovaries?

- ☐ A. Bilobed nuclei and inclusion-like nucleoli
- ☐ B. Intercellular bridges and keratin pearls
- ☐ C. Mucin-secreting signet cells
- ☐ D. Nests of epithelial cells with abundant clear cytoplasm
- ☐ E. Sebaceous glands and keratinaceous debris

**Submit**

Block Time Remaining: 00:34:08

TUTOR

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Feedback



Suspend



End Block





A 45-year-old woman comes to the office due to unintentional loss of 6.8 kg (15 lb) over the past 6 months. She used to enjoy dining with friends but now avoids it due to excessive lower abdominal pressure and feeling full very quickly. She also has epigastric pain but no dysphagia, regurgitation, vomiting, or diarrhea. Physical examination shows bilateral adnexal fullness. A pelvic ultrasound shows bilateral complex ovarian masses with solid and cystic components. Chest x-ray is normal. CT scan shows stomach wall thickening in addition to the ovarian masses. Which of the following is most likely to be seen on histologic evaluation of the ovaries?

- ☐ A. Bilobed nuclei and inclusion-like nucleoli (1%)
- ☐ B. Intercellular bridges and keratin pearls (3%)
- ☒ C. Mucin-secreting signet cells (78%)
- ☐ D. Nests of epithelial cells with abundant clear cytoplasm (10%)
- ☐ E. Sebaceous glands and keratinaceous debris (5%)





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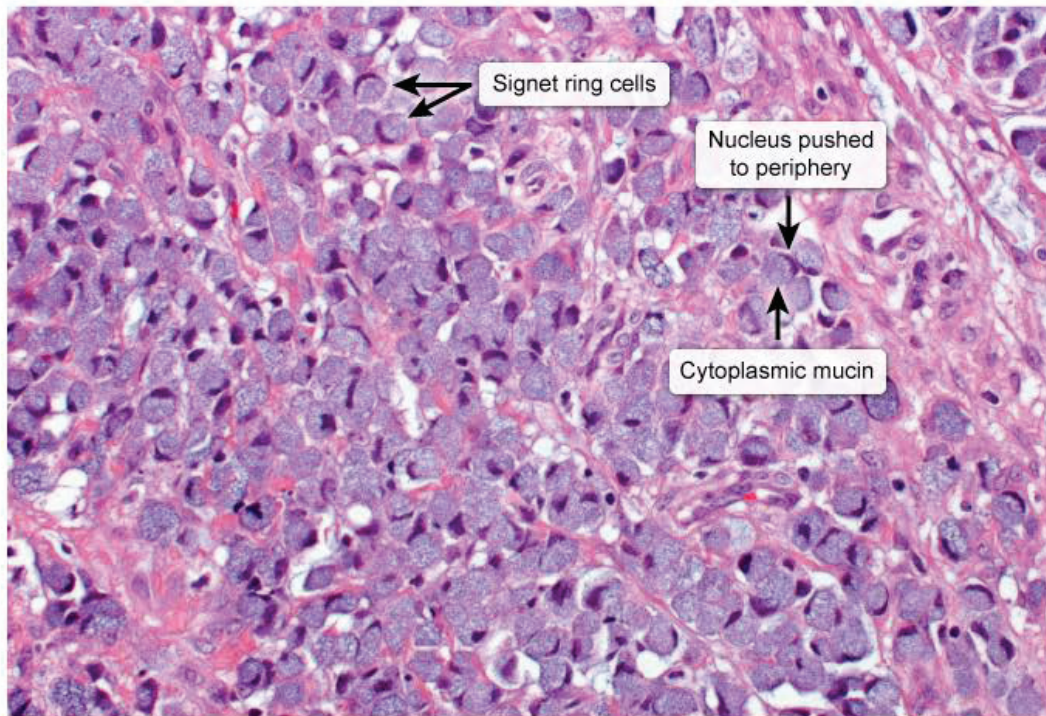


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Settings

### Metastatic gastric adenocarcinoma to ovary



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This patient's unintentional weight loss and early satiety are concerning for malignancy. The epigastric pain and gastric thickening on CT scan, as well as the lower abdominal pressure and adnexal masses, suggest gastric and ovarian involvement, respectively. The ovaries are a common site for metastases, often from a primary gastrointestinal tract cancer. This patient likely has a **Krukenberg tumor**, a primary **gastric cancer** that has **metastasized to the ovary**, often presenting with bilateral ovarian lesions. The cardinal histologic feature is nests of **signet ring cells**. The appearance is a result of large amounts of **mucin displacing the nucleus**.

Gastric signet ring cell cancer is particularly infiltrative and spreads to the ovaries by hematogenous or lymphatic invasion and peritoneal seeding. In contrast, primary ovarian and other cancers rarely metastasize to the stomach.

**(Choice A)** **Hodgkin lymphoma** is notable for Reed-Sternberg cells, which are derived from B cells and show bilobed ("owl's eye") or multiple nuclei and prominent inclusion-like nucleoli. Most patients have an enlarged lymph node in the neck or a mediastinal mass on chest x-ray, with no involvement of other organ systems.

**(Choice B)** Intercellular bridges are connections between squamous epithelial cells, and keratin pearls are



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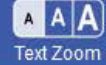
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systems.

**(Choice B)** Intercellular bridges are connections between squamous epithelial cells, and keratin pearls are whorl-shaped accumulations of keratin seen in **squamous cell carcinoma** (SCC). Common sites of SCC include the skin (eg, scaly patch or plaque on face), lung (cough, hemoptysis, chest pain, dyspnea), and middle third of the esophagus (dysphagia, unintentional weight loss).

**(Choice D)** Renal cell carcinoma causes the triad of flank pain, hematuria, and a palpable abdominal mass. **Clear cell carcinoma** is the most common type and appears as nests of epithelial cells with abundant clear cytoplasm separated by branching vascular tissue. This tumor spreads to the lungs and bone by invasion of the inferior vena cava without gastric or ovarian involvement.

**(Choice E)** Sebaceous glands and keratinaceous debris are histologic features of **mature cystic teratomas** of the ovaries, which are benign tumors that are most commonly asymptomatic or can cause torsion (acute pelvic pain) if very large.

### Educational objective:

A Krukenberg tumor is a gastric tumor that has metastasized to the ovary and can present with unintentional weight loss, epigastric pain, and adnexal masses. Histologically, the metastatic tumor cells have large amounts of mucin with displaced nuclei, resulting in a signet ring appearance.



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include the skin (eg, scaly patch or plaque on face), lung (cough, hemoptysis, chest pain, dyspnea), and middle third of the esophagus (dysphagia, unintentional weight loss).

**(Choice D)** Renal cell carcinoma causes the triad of flank pain, hematuria, and a palpable abdominal mass. **Clear cell carcinoma** is the most common type and appears as nests of epithelial cells with abundant clear cytoplasm separated by branching vascular tissue. This tumor spreads to the lungs and bone by invasion of the inferior vena cava without gastric or ovarian involvement.

**(Choice E)** Sebaceous glands and keratinaceous debris are histologic features of **mature cystic teratomas** of the ovaries, which are benign tumors that are most commonly asymptomatic or can cause torsion (acute pelvic pain) if very large.

### Educational objective:

A Krukenberg tumor is a gastric tumor that has metastasized to the ovary and can present with unintentional weight loss, epigastric pain, and adnexal masses. Histologically, the metastatic tumor cells have large amounts of mucin with displaced nuclei, resulting in a signet ring appearance.

### References

- **Isolated ovarian metastasis of gastric cancer: Krukenberg tumor.**
- **A curious discourse of Krukenberg tumor: a case report.**



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Settings

A 29-year-old woman comes to the office due to an intermittent nipple discharge for the past several weeks. She has had no fever or breast pain. The patient has never been pregnant despite having unprotected intercourse. She experienced menarche at age 12. Beginning a year ago, the patient's menses slowed to 2- to 3-month intervals and stopped completely 6 months ago. She has no other medical conditions and takes no medications. The patient's mother was diagnosed with metastatic breast cancer at age 60 and died recently. BMI is 31 kg/m<sup>2</sup>. On physical examination, white discharge is expressible from both nipples. The remainder of the physical examination is within normal limits. Urine  $\beta$ -hCG testing is negative. Which of the following is the most likely diagnosis in this patient?

- ☐ A. Fibroadenoma
- ☐ B. Fibrocystic changes of the breast
- ☐ C. Galactocele
- ☐ D. Inflammatory breast carcinoma
- ☐ E. Intraductal papilloma
- ☐ F. Lobular breast carcinoma



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menses slowed to 2- to 3-month intervals and stopped completely 6 months ago. She has no other medical conditions and takes no medications. The patient's mother was diagnosed with metastatic breast cancer at age 60 and died recently. BMI is 31 kg/m<sup>2</sup>. On physical examination, white discharge is expressible from both nipples. The remainder of the physical examination is within normal limits. Urine  $\beta$ -hCG testing is negative. Which of the following is the most likely diagnosis in this patient?

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- ☐ C. Galactocele
- ☐ D. Inflammatory breast carcinoma
- ☐ E. Intraductal papilloma
- ☐ F. Lobular breast carcinoma
- ☐ G. Paget disease of the breast
- ☐ H. Pituitary adenoma





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Settings

cancer at age 60 and died recently. BMI is 31 kg/m<sup>2</sup>. On physical examination, white discharge is expressible from both nipples. The remainder of the physical examination is within normal limits. Urine  $\beta$ -hCG testing is negative. Which of the following is the most likely diagnosis in this patient?

- ☐ A. Fibroadenoma (0%)
- ☐ B. Fibrocystic changes of the breast (1%)
- ☐ C. Galactocele (5%)
- ☐ D. Inflammatory breast carcinoma (0%)
- ☐ E. Intraductal papilloma (7%)
- ☐ F. Lobular breast carcinoma (0%)
- ☐ G. Paget disease of the breast (1%)
- ☒ H. Pituitary adenoma (82%)

Correct

82%



01 min, 07 secs



01/29/2021

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### Prolactinoma

<b>Clinical features</b>	<ul style="list-style-type: none"><li>• <b>Premenopausal women:</b> Oligomenorrhea/amenorrhea, infertility, galactorrhea, hot flashes, decreased bone density</li><li>• <b>Postmenopausal women:</b> Mass-effect symptoms (headache, visual field defects)</li><li>• <b>Men:</b> Infertility, decreased libido, impotence, gynecomastia</li></ul>
<b>Laboratory/ imaging</b>	<ul style="list-style-type: none"><li>• Serum prolactin (often &gt;200 ng/mL)</li><li>• Tests to rule out renal insufficiency (creatinine) &amp; hypothyroidism (TSH, thyroxine)</li><li>• MRI of the brain/pituitary</li></ul>
<b>Treatment</b>	<ul style="list-style-type: none"><li>• Dopamine agonist (cabergoline)</li><li>• Trans-sphenoidal surgery</li></ul>

**Galactorrhea** is the abnormal secretion of breast milk not associated with pregnancy or breastfeeding. It is most commonly due to excess prolactin, which directly stimulates milk secretion in the breasts.

**Hyperprolactinemia** also causes **amenorrhea** in women due to the inhibitory effect of prolactin on hypothalamic GnRH secretion.

Lactotroph adenomas (prolactinomas) are the most common hormonally active pituitary tumors and can





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Lactotroph adenomas (**prolactinomas**) are the most common hormonally active pituitary tumors and can cause very high prolactin levels. In addition, unlike most pituitary hormones, which are under positive regulation from the hypothalamus, prolactin is under **negative regulation** by hypothalamic dopaminergic neurons via the pituitary stalk, and any disruption of these pathways (eg, by a nonfunctioning pituitary adenoma) can cause moderate hyperprolactinemia.

In premenopausal women, such as this patient, prolactinomas typically present with galactorrhea and irregular menses. However, in men and postmenopausal women, early symptoms (eg, decreased libido) are often mild and nonspecific, and presentation typically occurs at a later stage with headaches and **bitemporal hemianopsia** due to compression of the optic chiasm in the **suprasellar region**. The diagnosis can be confirmed by **MRI of the brain**, and **dopamine agonists** (eg, bromocriptine, cabergoline) can be used to suppress prolactin secretion.

**(Choice A)** Fibroadenomas are benign neoplasms of the breast that often occur in young women. They present as a painless unilateral breast mass without nipple discharge.

**(Choice B)** Fibrocystic changes of the breast, a normal variant in which breasts feel dense and lumpy, commonly presents with cyclic mastalgia.

**(Choice C)** Galactocele, a mass filled with breast milk, can occur with hyperprolactinemia but is more



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**(Choice C)** Galactoceles, a mass filled with breast milk, can occur with hyperprolactinemia but is more often seen with normal lactation following pregnancy.

**(Choices D, F, and G)** Inflammatory breast carcinoma presents with diffuse breast induration, erythema, and peau d'orange (orange peel) skin due to blockage of lymphatic drainage by cancerous invasion. Lobular breast carcinoma typically presents as a painless breast mass. Paget disease is a manifestation of ductal carcinoma characterized by crusty, scaly redness on the nipple and areola with oozing and bleeding. Breast cancer may be associated with nipple discharge, but white galactorrhea is unusual, and menses are generally unaffected.

**(Choice E)** Intraductal papilloma is a benign tumor within the mammary duct. It is the most common cause of spontaneous nipple discharge, but the discharge is unilateral and typically bloody or serosanguineous.

### Educational objective:

Prolactinomas are the most common hormonally active pituitary adenomas. The excess prolactin produced by these tumors can cause galactorrhea and amenorrhea in premenopausal women. With a large mass, visual changes and headaches may occur due to compression of the optic chiasm.

### References

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Settings

A 16-year-old girl comes to the office due to 2 days of a burning sensation with urination. She had sexual intercourse with her partner last week and used a condom for contraception. The patient says, "I always urinate right after sex." She has no vaginal discharge, and vital signs are normal. Examination shows suprapubic tenderness. Urinalysis reveals positive nitrites, positive leukocyte esterase, 50 white blood cells/hpf, and many bacteria. Urine  $\beta$ -hCG is negative. Which of the following is the most likely cause of this patient's infection?

- ☐ A. Ascending infection
- ☐ B. Hematogenous spread of infection
- ☐ C. Lymphatic spread of infection
- ☐ D. Poor genital hygiene
- ☐ E. Sexually transmitted infection

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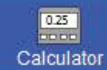


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- ☒ A. Ascending infection (83%)
- ☐ B. Hematogenous spread of infection (0%)
- ☐ C. Lymphatic spread of infection (0%)
- ☒ D. Poor genital hygiene (11%)
- ☐ E. Sexually transmitted infection (3%)

**Incorrect**

Correct answer

 83%  
Answered correctly 01 min, 08 secs  
Time Spent 09/04/2020  
Last Updated

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Settings

This patient's dysuria, suprapubic tenderness, and urinalysis abnormalities suggest **acute simple cystitis**.

Women are at much greater risk than men for urinary tract infections (UTIs) because they have a shorter urethra lying in close proximity to the anus and vaginal introitus, which allows **enteric flora** (eg, *Escherichia coli*) to spread to the vaginal opening and subsequently **ascend through the urethra to the bladder**. The major risk factor in otherwise healthy young women is recent **sexual intercourse**. Although urinating after intercourse flushes bacteria from the lower urinary tract (thereby reducing UTI risk), patients may still develop a UTI.

**(Choice B)** Hematologic infections generally enter the urinary tract through the glomeruli and cause pyelonephritis. Although pyuria and bacteriuria are usually present, most patients are systemically ill with fever, chills, and/or fatigue. Hematologic dissemination directly to the bladder is uncommon.

**(Choice C)** Lymphatic spread of infection is common in skin and soft tissue infections (eg, cellulitis) and is often marked by erythematous streaks on the skin. Lymphatic spread to the urinary tract system is uncommon.

**(Choice D)** Although poor genital hygiene can increase the risk that bacteria spread from the anus to the vaginal introitus, the primary mechanism of acute simple cystitis is the ascending spread of bacteria through the urethra to the bladder.



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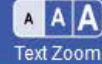
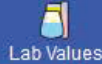
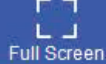
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uncommon.

**(Choice D)** Although poor genital hygiene can increase the risk that bacteria spread from the anus to the vaginal introitus, the primary mechanism of acute simple cystitis is the ascending spread of bacteria through the urethra to the bladder.

**(Choice E)** Sexually transmitted infections, particularly *Chlamydia trachomatis*, *Trichomonas vaginalis*, and *Neisseria gonorrhea*, often cause dysuria in women. However, these infections are frequently associated with vaginal discharge. In addition, suprapubic tenderness less common.

### Educational objective:

Women are at high risk for urinary tract infections due to a shorter urethra that is close to the anus and vaginal introitus, which allows enteric pathogens to colonize the vagina and ascend to the bladder. Acute simple cystitis is generally marked by dysuria, urinary frequency/urgency, suprapubic tenderness, and pyuria/bacteriuria on urinalysis.

Pathology

Female Reproductive System & Breast

Urinary tract infection

Subject

System

Topic

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Settings

A 55-year-old woman comes to the office due to vaginal bleeding. The patient underwent menopause at age 49 but has had intermittent, light vaginal bleeding for the last 6 months. She has no pelvic pain and otherwise feels well. The patient has type 2 diabetes mellitus, which is managed with diet and exercise. Vital signs are normal. BMI is 38 kg/m<sup>2</sup>. Speculum examination shows dark red blood at the cervical os. On bimanual examination, the uterus is small and nontender and there are no palpable adnexal masses. Which of the following is the most likely underlying cause of this patient's symptoms?

- ☐ A. Autonomous pituitary secretion of prolactin
- ☐ B. Ectopic implantation of endometrial glands and stroma
- ☐ C. Elevated sex-hormone binding globulin levels
- ☐ D. Increased peripheral aromatization of androgens
- ☐ E. Suppression of hypothalamic GnRH secretion

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Settings

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- ☐ A. Autonomous pituitary secretion of prolactin (0%)
- ☐ B. Ectopic implantation of endometrial glands and stroma (19%)
- ☐ C. Elevated sex-hormone binding globulin levels (6%)
- ☒ D. Increased peripheral aromatization of androgens (62%)
- ☐ E. Suppression of hypothalamic GnRH secretion (9%)

**Incorrect**

Correct answer:



62%

Answered correctly



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09/27/2020

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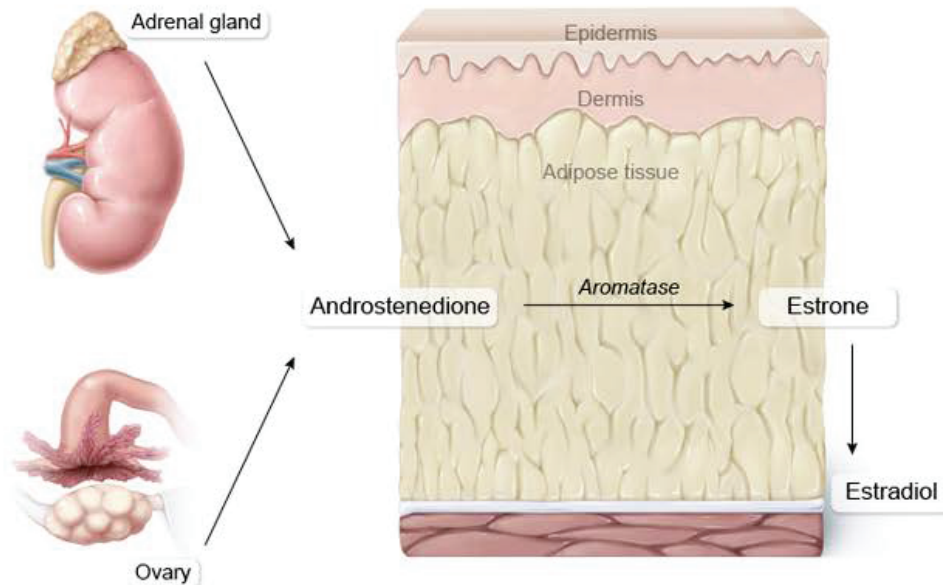
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## Exhibit Display

## Peripheral estrogen conversion in adipose tissue



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Settings

Ovary

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This obese patient with **postmenopausal bleeding** most likely has **endometrial hyperplasia or cancer**.

The most common risk factor for endometrial hyperplasia/cancer is chronic unopposed estrogen exposure, which is associated with **obesity**, early menarche, late menopause, and chronic anovulation.

Postmenopausal women have decreased ovarian function (ie, low estrogen and progesterone production), resulting in cessation of endometrial proliferation and subsequent amenorrhea. However, small amounts of androgens continue to be produced in the ovaries and adrenal glands after menopause. In obese women, these androgens (eg, androstenedione) are readily converted to estrogens (eg, estrone) by the **aromatase** enzyme found in **adipose tissue**.

The increased peripheral production of estrogens in adipose tissue and the decrease in sex-hormone binding globulin levels (that normally occurs with menopause) lead to elevated free estrogen levels **(Choice C)**. However, ovarian progesterone production remains low; therefore, the **unopposed estrogen** causes **unregulated endometrial proliferation** and subsequent endometrial hyperplasia or cancer, which often presents as postmenopausal or abnormal uterine bleeding.

**(Choice A)** Hyperprolactinemia due to autonomous pituitary secretion of prolactin (ie, pituitary adenoma) causes negative feedback to the **hypothalamus**. This results in decreased hypothalamic GnRH secretion

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often presents as postmenopausal or abnormal uterine bleeding.

**(Choice A)** Hyperprolactinemia due to autonomous pituitary secretion of prolactin (ie, pituitary adenoma) causes negative feedback to the [hypothalamus](#). This results in decreased hypothalamic GnRH secretion, decreased pituitary FSH and LH secretion, and decreased estrogen and progesterone levels. Therefore, premenopausal women often have signs of hyperprolactinemia (eg, galactorrhea) and hypoeestrogenism (eg, amenorrhea). In postmenopausal women, the most common symptom is tumor mass effect (eg, headache, bitemporal hemianopsia).

**(Choice B)** [Endometriosis](#), the ectopic implantation of endometrial glands and stroma, typically causes painful menses (ie, dysmenorrhea) due to inflamed tissue on the peritoneum. Endometriosis is uncommon after menopause because it requires high premenopausal estrogen levels that do not occur even in obese women.

**(Choice E)** Suppression of hypothalamic GnRH secretion (ie, hypothalamic hypogonadism) most commonly occurs in women with severe caloric restriction (eg, anorexia), excessive energy expenditure (eg, female athlete triad), or stress. The decreased GnRH secretion results in decreased pituitary FSH and LH secretion and subsequent decreased ovarian estrogen and progesterone production. Therefore, patients typically have amenorrhea rather than postmenopausal bleeding.







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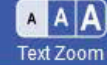
Notes



Calculator



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Settings

painful menses (ie, dysmenorrhea) due to inflamed tissue on the peritoneum. Endometriosis is uncommon after menopause because it requires high premenopausal estrogen levels that do not occur even in obese women.

**(Choice E)** Suppression of hypothalamic GnRH secretion (ie, hypothalamic hypogonadism) most commonly occurs in women with severe caloric restriction (eg, anorexia), excessive energy expenditure (eg, female athlete triad), or stress. The decreased GnRH secretion results in decreased pituitary FSH and LH secretion and subsequent decreased ovarian estrogen and progesterone production. Therefore, patients typically have amenorrhea rather than postmenopausal bleeding.

### Educational objective:

Endometrial hyperplasia and cancer often present with postmenopausal bleeding. A common risk factor for endometrial cancer is obesity due to the peripheral aromatization of androgens to estrogens in adipose tissue, which leads to chronic unopposed estrogen exposure and uncontrolled endometrial tissue proliferation.

### References

- [Addressing the role of obesity in endometrial cancer risk, prevention, and treatment.](#)



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Settings

A 30-year-old nulliparous woman comes to the office for evaluation of infertility. She has been attempting to conceive with her partner of 10 years for the past 2 years. Menarche was at age 11, and her menstrual cycles occur 2-3 times per year and last 7-10 days. The patient does not use tobacco, alcohol, or illicit drugs. Her blood pressure is 128/84 mm Hg and pulse is 84/min. BMI is 35 kg/m<sup>2</sup>. Physical examination shows mild acne and hair growth on the upper lip and chin. This patient is at greatest risk for which of the following complications?

- ☐ A. Adrenal atrophy
- ☐ B. Cushing syndrome
- ☐ C. Diabetes mellitus, type 1
- ☐ D. Endometrial carcinoma
- ☐ E. Vaginal adenosis

**Submit**

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Settings

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- ☐ A. Adrenal atrophy (6%)
- ☐ B. Cushing syndrome (10%)
- ☐ C. Diabetes mellitus, type 1 (9%)
- ☒ D. Endometrial carcinoma (69%)
- ☐ E. Vaginal adenosis (3%)

Correct

 69%  
Answered correctly 01 min, 11 secs  
Time Spent 02/19/2021  
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## Explanation

**Polycystic ovary syndrome****Clinical features**

- **Androgen excess:** Hirsutism, acne, androgenic alopecia
- **Ovarian dysfunction:** Menstrual irregularity, polycystic ovaries
- **Insulin resistance:** Acanthosis nigricans, glucose intolerance/diabetes, metabolic syndrome
- **Obesity**

**Treatment**

- Weight loss
- Combination hormonal contraceptives
- Metformin (if hyperglycemia/diabetes)

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This patient has **polycystic ovary syndrome (PCOS)**, a condition characterized by at least 2 of the following 3 criteria: signs of **hyperandrogenism**, **irregular periods**, and/or **polycystic ovaries on ultrasound**. PCOS results from increased activity of 17 $\alpha$ -hydroxylase; 17,20 lyase; and 3 $\beta$ -hydroxysteroid dehydrogenase. The overexpression of these enzymes results in elevated androgen levels (eg, testosterone, androstenedione, DHEA) and the clinical consequences of hirsutism and acne.

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- Metformin (if hyperglycemia/diabetes)

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This patient has **polycystic ovary syndrome (PCOS)**, a condition characterized by at least 2 of the following 3 criteria: signs of **hyperandrogenism**, **irregular periods**, and/or **polycystic ovaries on ultrasound**. PCOS results from increased activity of 17 $\alpha$ -hydroxylase; 17,20 lyase; and 3 $\beta$ -hydroxysteroid dehydrogenase. The overexpression of these enzymes results in elevated androgen levels (eg, testosterone, androstenedione, DHEA) and the clinical consequences of hirsutism and acne.

Excess androgen prevents development of a monthly dominant follicle, resulting in **anovulatory** cycles. In turn, menstrual irregularity (most often oligomenorrhea) results in **decreased progesterone** secretion. Progesterone has growth-inhibitory effects on the endometrium and counters estrogen-driven proliferation. The resulting imbalance of estrogen and progesterone places the patient with PCOS at long-term risk for **endometrial hyperplasia** and **adenocarcinoma**. In addition, anovulatory cycles often result in fertility difficulties as seen in this patient.

**(Choice A)** Autoimmune-mediated destructive adrenal atrophy is the most common cause of Addison disease, which presents as severe fatigue, weight loss, and low blood pressure due to glucocorticoid and mineralocorticoid deficiency. In contrast to PCOS, women may experience axillary and pubic hair loss due to adrenal androgen deficiency.

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Suspend

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Mark



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Lab Values



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Reverse Color



Text Zoom



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difficulties as seen in this patient.

**(Choice A)** Autoimmune-mediated destructive adrenal atrophy is the most common cause of Addison disease, which presents as severe fatigue, weight loss, and low blood pressure due to glucocorticoid and mineralocorticoid deficiency. In contrast to PCOS, women may experience axillary and pubic hair loss due to adrenal androgen deficiency.

**(Choice B)** Patients with Cushing syndrome have symptoms similar to those of patients with PCOS such as obesity, menstrual irregularities, and increased body hair. However, hypertension, abdominal striae, and supraclavicular fat pads are also typically seen in Cushing syndrome due to excess cortisol.

**(Choice C)** PCOS is a risk factor for type 2 diabetes mellitus (T2DM) due to increased insulin resistance. In contrast, patients with a family history of T1DM are at increased risk of developing T1DM, which results from decreased insulin secretion.

**(Choice E)** Vaginal adenosis is the persistence of glandular columnar epithelium in the vagina and is a precursor for clear cell adenocarcinoma of the vagina. Female offspring exposed to diethylstilbestrol in utero are at increased risk and may present with vaginal discharge or vaginal cysts/fleshy colored lesions.

### Educational objective:

Polycystic ovary syndrome (PCOS) is associated with oligomenorrhea, hirsutism, and polycystic ovaries.

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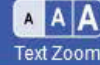
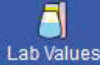
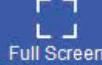


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**(Choice C)** PCOS is a risk factor for type 2 diabetes mellitus (T2DM) due to increased insulin resistance. In contrast, patients with a family history of T1DM are at increased risk of developing T1DM, which results from decreased insulin secretion.

**(Choice E)** Vaginal adenosis is the persistence of glandular columnar epithelium in the vagina and is a precursor for clear cell adenocarcinoma of the vagina. Female offspring exposed to diethylstilbestrol in utero are at increased risk and may present with vaginal discharge or vaginal cysts/fleshy colored lesions.

### Educational objective:

Polycystic ovary syndrome (PCOS) is associated with oligomenorrhea, hirsutism, and polycystic ovaries. Disruption in intraovarian steroidogenesis causes anovulatory cycles and results in chronic estrogen stimulation with decreased progesterone secretion, placing PCOS patients at risk for endometrial hyperplasia/carcinoma.

### References

- ACOG Practice Bulletin No. 108: Polycystic Ovary Syndrome.
- Catch It Before It Kills: Progesterone, Obesity, and the Prevention of Endometrial Cancer





A 38-year-old woman comes to the emergency department for lower abdominal pain. The patient has had some mild, cramping abdominal pain for the past few days, but today it became constant. She has also had intermittent vaginal bleeding. The patient has a history of irregular menses, and her last menstrual period was 8 weeks ago. Physical examination shows a left adnexal mass. The patient undergoes surgery and the resected specimen is shown in the image below:





Which of the following risk factors is most strongly associated with this patient's condition?

☐ A. Family history of ovarian cancer



Which of the following risk factors is most strongly associated with this patient's condition?

- ☐ A. Family history of ovarian cancer
- ☐ B. Müllerian anomaly
- ☐ C. Prior pelvic surgery
- ☐ D. Progestin-only oral contraceptive use
- ☐ E. Recent anticoagulant use

Submit

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Which of the following risk factors is most strongly associated with this patient's condition?

- ☐ A. Family history of ovarian cancer (12%)
- ☐ B. Müllerian anomaly (8%)
- ☒ C. Prior pelvic surgery (64%)
- ☐ D. Progestin-only oral contraceptive use (10%)
- ☐ E. Recent anticoagulant use (3%)

Correct

64%



54 secs



09/19/2020

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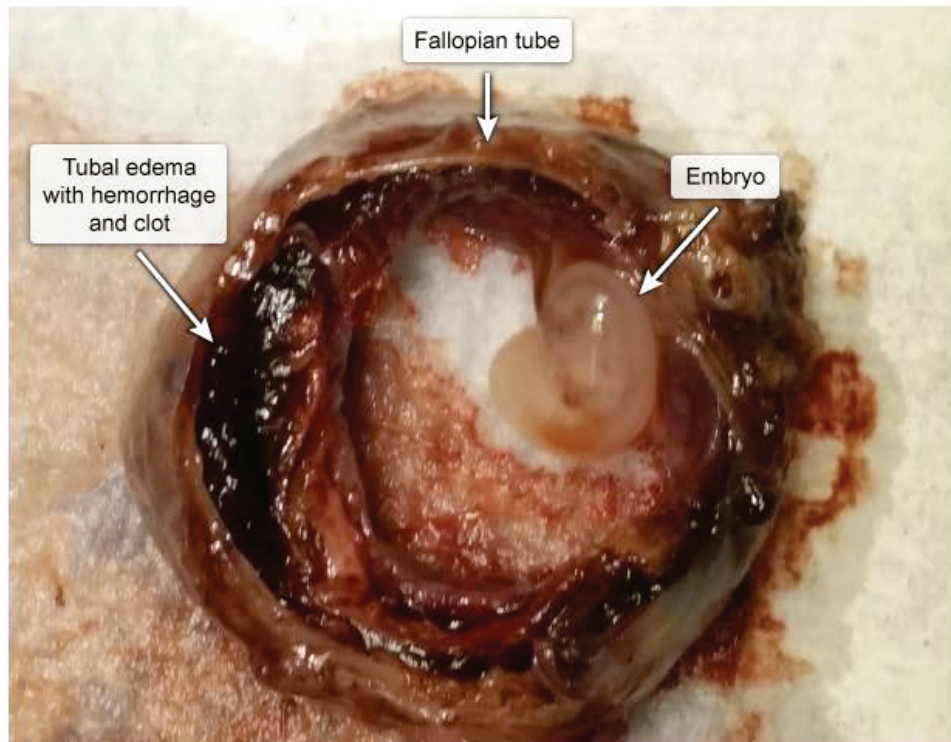
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### Ectopic pregnancy





This patient with lower abdominal cramping, vaginal bleeding, and a palpable adnexal mass has an **ectopic pregnancy** (ie, embryo implantation in an extrauterine location [most commonly the **fallopian tube**]). The surgical specimen above reveals products of conception (eg, embryo) surrounded by the fallopian tube wall, which is grossly intact but edematous with evidence of hemorrhage (ie, blood clots) due to tubal injury.

The fallopian tube, specifically the ampulla, is the most common site of ectopic pregnancy due to high rates of **tubal scarring** among reproductive-aged women. Tubal scarring impedes the migration of the embryo past the abnormally scarred segment and promotes tubal rather than uterine implantation. **Risk factors** associated with tubal scarring include prior ectopic pregnancy, pelvic inflammatory disease, and **prior pelvic surgery** (eg, tubal ligation). Other risk factors for ectopic pregnancy include tobacco use (due to decreased tubal motility) and in vitro fertilization.

**(Choice A)** Family history of ovarian cancer due to an inherited mutation (eg, *BRCA*) can increase the risk of ovarian cancer but does not affect the risk of ectopic pregnancy.

**(Choice B)** **Müllerian anomalies** typically cause agenesis or hypoplasia of the fallopian tubes, uterus, cervix, or vagina. Therefore, patients are at increased risk for infertility and spontaneous abortion rather than ectopic pregnancy.







Mark



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of ovarian cancer but does not affect the risk of ectopic pregnancy.

**(Choice B)** Müllerian anomalies typically cause agenesis or hypoplasia of the fallopian tubes, uterus, cervix, or vagina. Therefore, patients are at increased risk for infertility and spontaneous abortion rather than ectopic pregnancy.

**(Choice D)** Progestin-only oral contraceptives decrease, not increase, the risk for ectopic pregnancy by preventing ovulation and thickening the cervical mucus to prevent sperm entry.

**(Choice E)** Recent anticoagulant use is a risk factor for hemorrhagic ovarian cysts, which develop due to bleeding into a physiologic ovarian cyst and can cause severe abdominal pain with cyst rupture. Hemorrhagic cysts are typically thin-walled and filled with blood or clot; there are no associated products of conception.

### Educational objective:

Ectopic pregnancy occurs when the embryo implants in an extrauterine location, most commonly the fallopian tube. Risk factors for ectopic pregnancy include tubal scarring (eg, prior pelvic surgery, pelvic inflammatory disease), tobacco use, and in vitro fertilization.

### References

- [Incidence, diagnosis and management of tubal and nontubal ectopic pregnancies: a review.](#)



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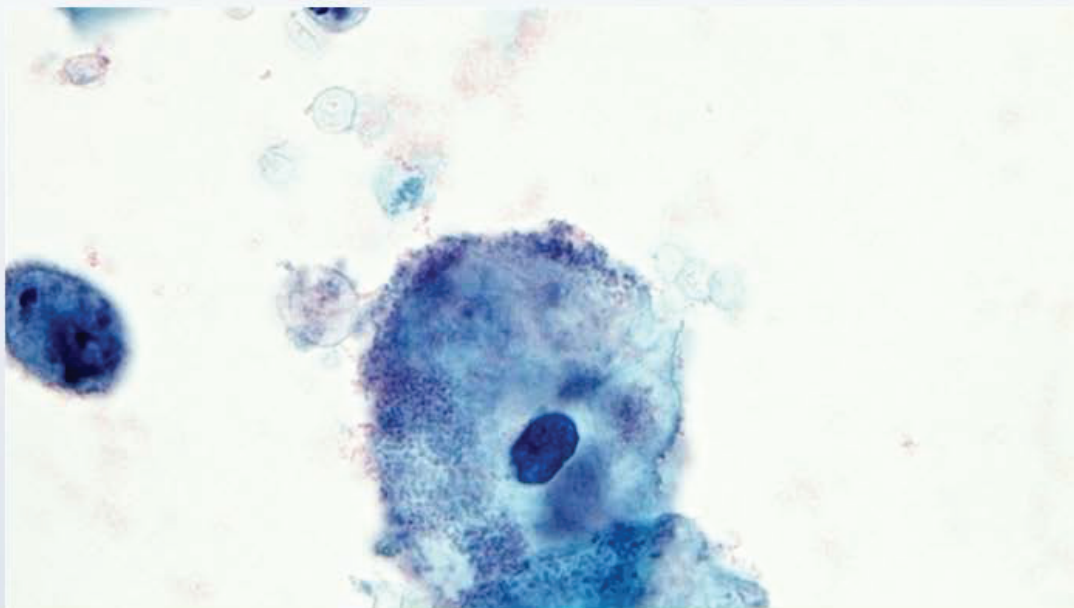


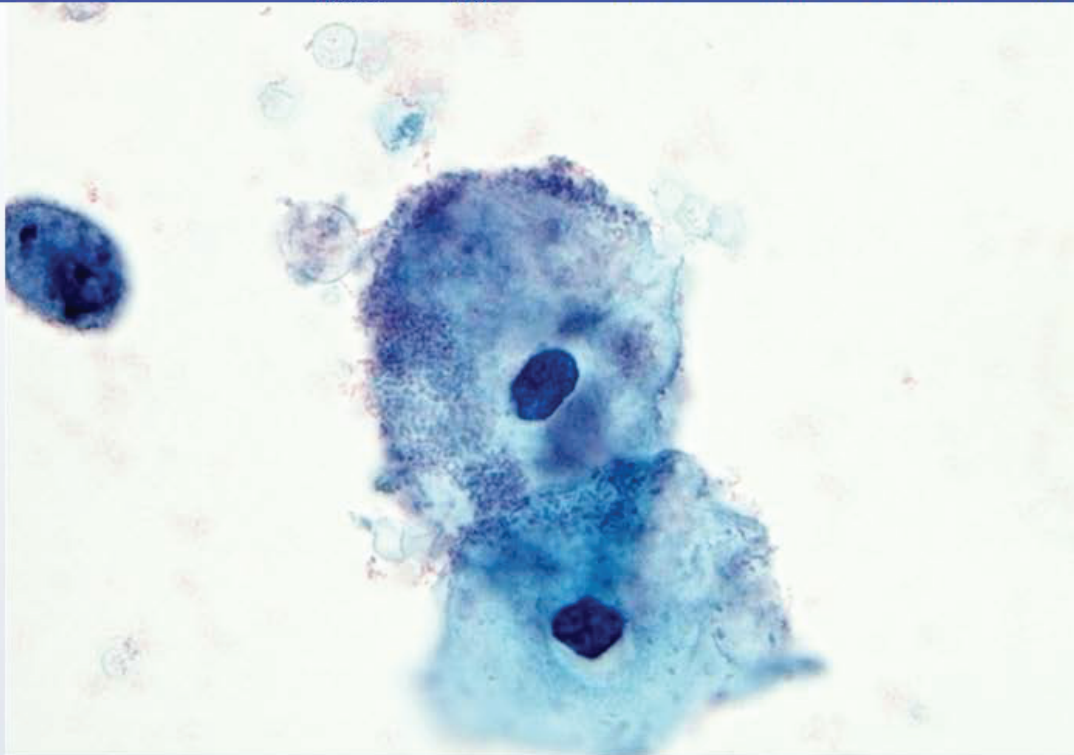
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End Block

A 32-year-old woman, gravida 1 para 1, comes to the office for vaginal discharge. The patient has no chronic medical conditions and takes no daily medications. Her last menstrual period was 3 weeks ago. The patient has recently become sexually active with a new partner and uses an intrauterine device for contraception. Cytology of the discharge is shown in the image below:





Which of the following best describes the predominant organism causing this patient's condition?

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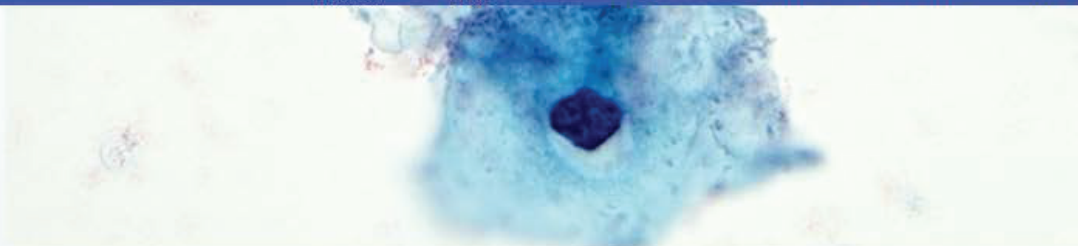
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Which of the following best describes the predominant organism causing this patient's condition?

- ☐ A. Anaerobic gram-variable rod
- ☐ B. Diploid fungus
- ☐ C. Gram-negative diplococcus
- ☐ D. Intracellular gram-negative bacterium
- ☐ E. Motile protozoan
- ☐ F. Naked DNA virus

**Submit**

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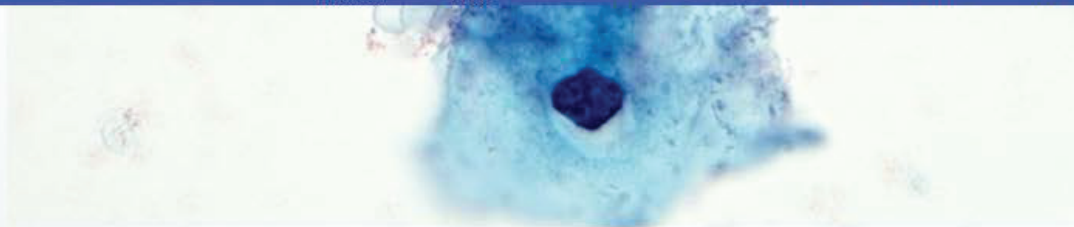
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Which of the following best describes the predominant organism causing this patient's condition?

- ☒ A. Anaerobic gram-variable rod (56%)
- ☐ B. Diploid fungus (2%)
- ☐ C. Gram-negative diplococcus (6%)
- ☐ D. Intracellular gram-negative bacterium (13%)
- ☐ E. Motile protozoan (9%)
- ☐ F. Naked DNA virus (11%)

Correct

56%

59 secs

10/14/2020

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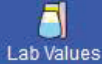
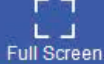
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**Bacterial vaginosis** (BV) is most commonly caused by an overgrowth of the facultative **anaerobic, gram-variable rod** *Gardnerella vaginalis* and loss of normal lactobacilli flora. A classic symptom is a thin, malodorous, grayish-white vaginal discharge. The odor becomes more prominent with the addition of potassium hydroxide (**whiff test**) to a sample due to the anaerobes that release amines. Wet mount microscopy of the discharge and cytologic smears characteristically show **blue cells**, which are **vaginal squamous epithelial cells** covered with multiple, small, **adherent G vaginalis** organisms. Treatment is with metronidazole or clindamycin.

**(Choice B)** *Candida albicans* vaginitis is associated with intense vaginal pruritus; white, curd-like discharge; and labial erythema. Pseudohyphae of this diploid fungus are seen on potassium hydroxide preparations of the vaginal discharge.

**(Choices C and D)** *Neisseria gonorrhoeae* and *Chlamydia trachomatis* are transmitted sexually, commonly together. These organisms can cause cervicitis, which typically presents with a mucopurulent cervical discharge. Microscopy of *N gonorrhoeae* shows gram-negative intracellular diplococci, and *C trachomatis* microscopy is typically normal or shows leukocytes.

**(Choice E)** *Trichomonas vaginalis* is a flagellated protozoan that causes trichomoniasis, which is







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Settings

commonly together. These organisms can cause cervicitis, which typically presents with a mucopurulent cervical discharge. Microscopy of *N gonorrhoeae* shows gram-negative intracellular diplococci, and *C trachomatis* microscopy is typically normal or shows leukocytes.

**(Choice E)** *Trichomonas vaginalis* is a flagellated protozoan that causes trichomoniasis, which is associated with a yellow-green, frothy discharge. Motile, flagellated trophozoites are seen on wet mount microscopy.

**(Choice F)** Human papillomavirus is a naked DNA virus that can cause condylomata acuminata and cervical cancer. Condylomata are commonly caused by strains 6 and 11, and oncogenic strains include types 16 and 18. Human papillomavirus infections do not typically cause vaginal discharge.

### Educational objective:

Bacterial vaginosis is associated with a grayish-white, malodorous vaginal discharge due to an overgrowth of *Gardnerella vaginalis*, a facultative anaerobic, gram-variable rod. Clue cells (squamous epithelial cells covered with bacterial organisms) are seen on wet mount microscopy or cytology.

Microbiology

Female Reproductive System &amp; Breast

Bacterial vaginosis

Subject

System

Topic

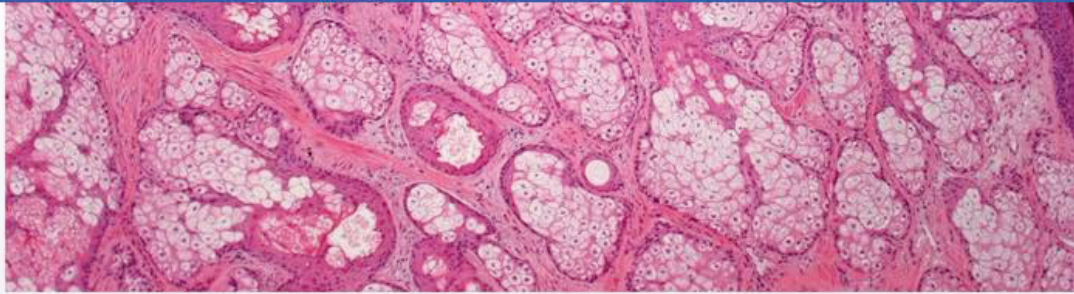
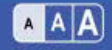
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Which of the following is the most likely diagnosis?

- ☐ A. Ectopic pregnancy (3%)
- ☐ B. Endometriosis (13%)
- ☐ C. High-grade serous ovarian carcinoma (34%)
- ☒ D. Mature teratoma (38%)
- ☐ E. Polycystic ovary syndrome (10%)

Correct

38%



01 min, 20 secs



02/07/2021

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### Mature teratoma of the ovary







This patient has a **mature teratoma**, the most common subtype of ovarian germ cell neoplasm. They are primarily found in women age 10-30. Most patients are asymptomatic and found to have an incidental mass on pelvic examination or ultrasound, but some can present with pain or abdominal discomfort.

Teratomas are characterized by the presence of tissue from **multiple germ layers** (ectoderm, mesoderm, and endoderm). Morphologically, they are subclassified as **benign** mature teratomas (contain mature tissue) and malignant immature teratomas (contain mature and immature tissue, commonly fetal neuroepithelium).

Mature teratomas are **cystic** lesions and may contain sebaceous content, hair, and teeth. By microscopy, diverse tissues can be seen, including skin (eg, **hair follicles**, **sebaceous glands**), bone, respiratory epithelium, and thyroid tissue. Although mature teratomas are benign, they may seldom develop malignant change (eg, squamous cell carcinoma).

**(Choice A)** In **ectopic pregnancy**, the blastocyst implants outside the endometrial cavity (eg, fallopian tube). It can be diagnosed with transvaginal ultrasonography and  $\beta$ -hCG measurements. Although ectopic pregnancy may present with abdominal pain, histologic evaluation of the mass would reveal chorionic villi.

**(Choice B)** **Endometriosis** is characterized by endometrial tissue implanted outside the uterine cavity.

Ovarian endometriosis may present with abdominal pain and an adnexal mass; however, microscopic





pregnancy may present with abdominal pain, histologic evaluation of the mass would reveal chorionic villi.

**(Choice B)** **Endometriosis** is characterized by endometrial tissue implanted outside the uterine cavity.

Ovarian endometriosis may present with abdominal pain and an adnexal mass; however, microscopic examination would show endometrial glands and stroma.

**(Choice C)** **High-grade serous ovarian carcinoma** usually presents in older women. Typical histologic features include ovarian stromal invasion by atypical cells (pleomorphic, large, irregular nuclei and prominent nucleoli) forming papillae and glandular spaces.

**(Choice E)** Polycystic ovary syndrome presents with clinical/biochemical evidence of hyperandrogenism and oligo/anovulation. Ultrasound would reveal polycystic ovaries (rather than a unilateral adnexal mass), and microscopy would reveal cystic follicles and stromal fibrosis.

### Educational objective:

Teratomas are the most common subtype of ovarian germ cell neoplasms and occur most frequently in women age 10-30. Mature teratomas are benign and show mature tissues derived from multiple germ layers, frequently including skin, hair, and teeth.

### References

- [Germ cell tumors of the gonads: a selective review emphasizing problems in differential diagnosis](#)





A 24-year-old woman comes to the office for an infertility evaluation. The patient has had irregular menstrual cycles for the past 5 years, with menstrual periods every 2-3 months. Medical history is notable for an appendectomy 8 years ago but is otherwise not significant. The patient takes no medications. Blood pressure is 125/86 mm Hg and pulse is 72/min. BMI is 33 kg/m<sup>2</sup>. Physical examination shows facial acne and excessive hair growth on the upper lip and chin. Which of the following pathologic findings is most likely to be seen in this patient?

- ☐ A. Atrophic endometrium
- ☐ B. Bilateral adrenal atrophy
- ☐ C. Enlarged ovaries
- ☐ D. Pituitary adenoma
- ☐ E. Polycystic kidneys

Submit







A 24-year-old woman comes to the office for an **infertility evaluation**. The patient has had irregular menstrual cycles for the past 5 years, with menstrual periods every 2-3 months. Medical history is notable for an **appendectomy** 8 years ago but is otherwise not significant. The patient takes no medications. Blood pressure is 125/86 mm Hg and pulse is 72/min. **BMI** is 33 kg/m<sup>2</sup>. Physical examination shows facial **acne** and excessive hair growth on the upper lip and chin. Which of the following pathologic findings is most likely to be seen in this patient?

- ☐ A. Atrophic endometrium (0%)
- ☐ B. Bilateral adrenal atrophy (0%)
- ☒ C. Enlarged ovaries (100%)
- ☐ D. Pituitary adenoma (0%)
- ☒ E. Polycystic kidneys (0%)

**Incorrect**

Correct answer

Collecting Statistics



42 secs

Time Spent



04/01/2021

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End Block



### Polycystic ovary syndrome

#### Clinical features

- Androgen excess (eg, acne, male pattern baldness, hirsutism)
- Oligoovulation or anovulation (eg, menstrual irregularities)
- Obesity
- Polycystic ovaries on ultrasound

#### Pathophysiology

- ↑ Testosterone levels
- ↑ Estrogen levels
- LH/FSH imbalance

This patient with menstrual irregularities, infertility, obesity, and hirsutism likely has **polycystic ovary syndrome (PCOS)**. The etiology is heterogeneous and multifactorial (eg, hormonal, genetic, environmental), but patients characteristically have elevated levels of both androgen and estrogen.

**Hyperandrogenism**, which can be diagnosed clinically (eg, hirsutism, acne) or biochemically (ie, elevated testosterone), occurs due to increased ovarian androgen production. Androgens are then converted to estrogens in the peripheral adipose tissue and ovaries by the enzyme aromatase; patients with PCOS are commonly **obese** and have **increased** peripheral and ovarian **estrogen production** (ie, estrone and





commonly **obese** and have increased peripheral and ovarian **estrogen production** (ie, estrone and estradiol).

The consistent elevation in estrogen acts on the hypothalamic-pituitary-ovarian axis and causes **menstrual irregularities** and anovulatory infertility. During a **normal menstrual cycle**, the growth of a dominant follicle causes a gradual increase in estrogen, which triggers hypothalamic GnRH release in a high-frequency pulse pattern that preferentially stimulates greater LH than FSH production in the anterior pituitary (ie, the LH surge to trigger oocyte release). Following ovulation, GnRH release returns to a low-frequency pattern that allows FSH to stimulate the next follicular phase.

In contrast, patients with PCOS have consistently elevated estrogen levels, leading to a **persistent imbalance in the LH/FSH ratio**. Because FSH remains low relative to LH, there is no maturation and release of a single, dominant ovarian follicle (ie, **anovulation**). Instead, multiple, smaller follicles accumulate fluid to cause the **classic appearance** of **bilateral, enlarged, polycystic ovaries**.

**(Choice A)** Endometrial proliferation is estrogen dependent. An atrophic endometrium is associated with low estrogen (eg, menopause); in contrast, patients with PCOS have chronically elevated estrogen levels and are at increased risk for endometrial hyperplasia or cancer.

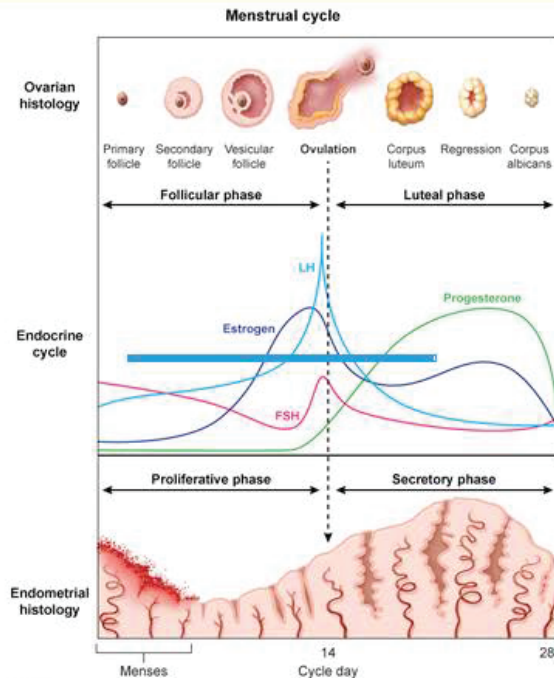
**(Choices B and D)** Cushing syndrome is caused by cortisol excess, usually due to a hyperfunctioning adrenal adenoma (which causes compensatory contralateral, not bilateral, adrenal atrophy) or an ACTH





commonly obese and have increased peripheral and ovarian estrogen production (ie, estrone and

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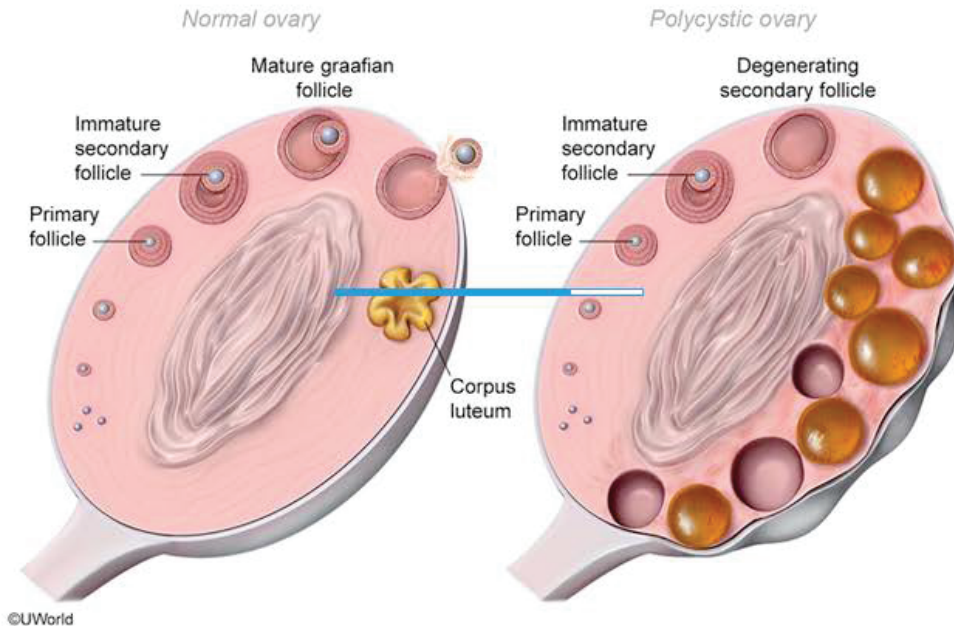
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commonly obese and have increased peripheral and ovarian estrogen production (ie, estrone and

## Exhibit Display

## Polycystic ovary syndrome



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Zoom In



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**(Choice A)** Endometrial proliferation is estrogen dependent. An atrophic endometrium is associated with low estrogen (eg, menopause); in contrast, patients with PCOS have chronically elevated estrogen levels and are at increased risk for endometrial hyperplasia or cancer.

**(Choices B and D)** Cushing syndrome is caused by cortisol excess, usually due to a hyperfunctioning adrenal adenoma (which causes compensatory contralateral, not bilateral, adrenal atrophy) or an ACTH-producing pituitary adenoma. Although Cushing syndrome and PCOS share several clinical features (eg, obesity, hirsutism, menstrual irregularities), patients with Cushing syndrome typically also have moon facies, enlarged fat pads, hypertension, and proximal muscle weakness.

**(Choice E)** Polycystic kidney disease is an inherited condition with juvenile and adult forms. Patients typically have hypertension, flank pain, hematuria, and renal insufficiency. It does not cause menstrual irregularities or hirsutism.

### Educational objective:

Polycystic ovary syndrome (PCOS) may present with menstrual irregularities, signs of hyperandrogenism (eg, acne, hirsutism), and obesity. Patients with PCOS typically have bilateral, enlarged, cystic ovaries.

### References

- [Genetic, hormonal and metabolic aspects of PCOS: an update.](#)

